



Clinical trial results:

A Phase 1 Dose Escalation and Phase 2 Randomized Double-Blind Study of Veliparib in Combination with Carboplatin and Etoposide as a Therapy of Treatment-Naïve Extensive Stage Disease Small Cell Lung Cancer

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2014-001764-35 |
| Trial protocol | ES NL CZ BE HU FR |
| Global end of trial date | 17 April 2019 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 22 May 2020 |
| First version publication date | 30 April 2020 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Need to correct a table in the safety section of the report. |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | M14-361 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02289690 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Abbvie Deutschland GmbH & Co.KG |
| Sponsor organisation address | AbbVie House, Vanwall Business Park, Maidenhead, Berkshire, United Kingdom, SL6-4UB |
| Public contact | Global Medical Services, AbbVie, 011 800-633-9110, |
| Scientific contact | Bruce Bach, MD, AbbVie, bruce.bach@abbvie.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|---------------|
| Analysis stage | Final |
| Date of interim/final analysis | 17 April 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 April 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the Phase 1 dose-escalation were:

- To establish the maximum tolerated dose (MTD) and to establish the recommended Phase 2 dose (RPTD) and schedule for veliparib in combination with carboplatin and etoposide.
- To evaluate the pharmacokinetic (PK) interaction between veliparib and etoposide.

The primary objective of Phase 2 was:

- To evaluate if veliparib in combination with carboplatin and etoposide followed by veliparib maintenance monotherapy results in improved progression-free survival vs. placebo in combination with carboplatin and etoposide followed by placebo monotherapy in subjects with treatment-naïve extensive stage small-cell lung cancer (ED SCLC).

Protection of trial subjects:

All subjects entering the study had to sign an informed consent that was explained to them and questions encouraged.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 13 October 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Spain: 24 |
| Country: Number of subjects enrolled | United States: 44 |
| Country: Number of subjects enrolled | Australia: 1 |
| Country: Number of subjects enrolled | Belgium: 12 |
| Country: Number of subjects enrolled | Canada: 5 |
| Country: Number of subjects enrolled | Czech Republic: 6 |
| Country: Number of subjects enrolled | France: 10 |
| Country: Number of subjects enrolled | Hungary: 24 |
| Country: Number of subjects enrolled | Korea, Republic of: 17 |
| Country: Number of subjects enrolled | Netherlands: 36 |
| Country: Number of subjects enrolled | Romania: 1 |
| Country: Number of subjects enrolled | Russian Federation: 41 |
| Worldwide total number of subjects | 221 |
| EEA total number of subjects | 113 |

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) | 131 |
| From 65 to 84 years | 88 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 52 study sites located in 12 countries (Australia, Belgium, Canada, Czech Republic, France, Hungary, Korea, the Netherlands, Romania, Russian Federation, Spain, United States).

Pre-assignment

Screening details:

Participants in Phase 1 were sequentially assigned to ascending dose levels of veliparib in combination with standard carboplatin/etoposide regimen. Participants in Phase 2 were randomized equally to placebo, carboplatin/etoposide followed by placebo maintenance, or to veliparib, carboplatin/etoposide followed by veliparib or placebo maintenance.

Period 1

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

Blinding implementation details:

Phase 1 was open-label. Participants in Phase 2 were randomized using an Interactive Response Technology (IRT) system. All study site personnel, including the investigator, study coordinator, as well as the subjects, remained blinded to the treatment throughout the course of the Phase 2 portion of the study.

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Etoposide |

Arm description:

Participants received 80 mg veliparib orally twice a day (BID) on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered intravenously (IV) on Day 1 at a target area under the curve (AUC) 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Veliparib |
| Investigational medicinal product code | ABT-888 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Capsules administered orally twice a day according to the dosing schedule.

| | |
|------------------|--|
| Arm title | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Etoposide |
|------------------|--|

Arm description:

Participants received 120 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

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

| | |
|--|-----------|
| Investigational medicinal product name | Veliparib |
| Investigational medicinal product code | ABT-888 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Capsules administered orally twice a day according to the dosing schedule.

| | |
|------------------|--|
| Arm title | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Etoposide |
|------------------|--|

Arm description:

Participants received 160 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Veliparib |
| Investigational medicinal product code | ABT-888 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Capsules administered orally twice a day according to the dosing schedule.

| | |
|------------------|--|
| Arm title | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Etoposide |
|------------------|--|

Arm description:

Participants received 200 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Veliparib |
| Investigational medicinal product code | ABT-888 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Capsules administered orally twice a day according to the dosing schedule.

| | |
|------------------|--|
| Arm title | Phase 1: Veliparib 240 mg BID 7 Days + Carboplatin/Etoposide |
|------------------|--|

Arm description:

Participants received 240 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

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

| | |
|--|-----------|
| Investigational medicinal product name | Veliparib |
| Investigational medicinal product code | ABT-888 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Capsules administered orally twice a day according to the dosing schedule.

| | |
|------------------|---|
| Arm title | Phase 1: Veliparib 240 mg BID 14 Days + Carboplatin/Etoposide |
|------------------|---|

Arm description:

Participants received 240 mg veliparib orally BID on Days -2 to 12 (14 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 12 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Veliparib |
| Investigational medicinal product code | ABT-888 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Capsules administered orally twice a day according to the dosing schedule.

| | |
|------------------|---|
| Arm title | Phase 1: Veliparib 240 mg BID 21 Days + Carboplatin/Etoposide |
|------------------|---|

Arm description:

Participants received 240 mg veliparib orally BID on Days -2 to Day 19 (continuous schedule) in combination with carboplatin/etoposide for up to four 21-day cycles. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Veliparib |
| Investigational medicinal product code | ABT-888 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Capsules administered orally twice a day according to the dosing schedule.

| | |
|------------------|---|
| Arm title | Phase 2: Veliparib + Carboplatin/Etoposide -> Veliparib |
|------------------|---|

Arm description:

Participants in Arm A received veliparib 240 mg BID on Day -2 to 12 (14-day schedule), carboplatin AUC 5 mg/mL*min administered on Day 1, and etoposide 100 mg/m² administered on Days 1 to 3 of each 21-day cycle for up to 6 cycles.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Veliparib |
| Investigational medicinal product code | ABT-888 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Veliparib capsules administered orally twice a day according to the dosing schedule.

| | |
|------------------|---|
| Arm title | Phase 2: Veliparib + Carboplatin/Etoposide -> Placebo |
|------------------|---|

Arm description:

Participants In Arm B received veliparib 240 mg BID on Day -2 to 12 (14-day schedule), carboplatin AUC 5 mg/mL*min administered on Day 1, and etoposide 100 mg/m² administered on Days 1 to 3 of each 21-day cycle for up to 6 cycles.

Participants without evidence of disease progression received placebo monotherapy BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Veliparib |
| Investigational medicinal product code | ABT-888 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Veliparib capsules administered orally twice a day according to the dosing schedule.

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

Dosage and administration details:

Placebo capsules administered orally twice a day according to the dosing schedule.

| | |
|------------------|---|
| Arm title | Phase 2: Placebo + Carboplatin/Etoposide -> Placebo |
|------------------|---|

Arm description:

Participants in Arm C received placebo BID on Day -2 to 12 (14-day schedule), carboplatin AUC 5 mg/mL*min on Day 1, and etoposide 100 mg/m² on Days 1 to 3 of each 21-day cycle for up to 6 cycles. Participants without evidence of disease progression received placebo monotherapy BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo capsules administered orally twice a day according to the dosing schedule.

| Number of subjects in period 1 | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Etoposide |
|---------------------------------------|---|--|--|
| Started | 4 | 3 | 4 |
| Received Study Drug | 4 | 3 | 4 |

| | | | |
|--------------------------------------|---|---|---|
| Completed | 0 | 0 | 0 |
| Not completed | 4 | 3 | 4 |
| Adverse Event Related to Progression | - | 1 | 1 |
| Consent withdrawn by subject | 1 | - | - |
| Other | - | - | - |
| Death | - | - | - |
| Sponsor Discontinued Study | - | - | - |
| Progressive Disease, Per Protocol | 3 | 2 | 3 |
| Lost to follow-up | - | - | - |

| Number of subjects in period 1 | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 240 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 240 mg BID 14 Days + Carboplatin/Etoposide |
|---------------------------------------|---|---|--|
| Started | 3 | 8 | 14 |
| Received Study Drug | 3 | 8 | 14 |
| Completed | 0 | 0 | 0 |
| Not completed | 3 | 8 | 14 |
| Adverse Event Related to Progression | - | 1 | - |
| Consent withdrawn by subject | - | 1 | 1 |
| Other | 1 | 1 | - |
| Death | - | - | - |
| Sponsor Discontinued Study | - | - | - |
| Progressive Disease, Per Protocol | 2 | 5 | 13 |
| Lost to follow-up | - | - | - |

| Number of subjects in period 1 | Phase 1: Veliparib 240 mg BID 21 Days + Carboplatin/Etoposide | Phase 2: Veliparib + Carboplatin/Etoposide -> Veliparib | Phase 2: Veliparib + Carboplatin/Etoposide -> Placebo |
|---------------------------------------|--|--|--|
| Started | 4 | 61 | 59 |
| Received Study Drug | 4 | 60 | 58 |
| Completed | 0 | 0 | 0 |
| Not completed | 4 | 61 | 59 |
| Adverse Event Related to Progression | 1 | - | - |
| Consent withdrawn by subject | - | - | 4 |
| Other | 1 | 2 | 3 |
| Death | - | 49 | 45 |
| Sponsor Discontinued Study | - | 9 | 7 |
| Progressive Disease, Per Protocol | 2 | - | - |
| Lost to follow-up | - | 1 | - |

| Number of subjects in period 1 | Phase 2: Placebo + Carboplatin/Etoposide |
|---------------------------------------|---|
|---------------------------------------|---|

| | e -> Placebo |
|--------------------------------------|--------------|
| Started | 61 |
| Received Study Drug | 60 |
| Completed | 0 |
| Not completed | 61 |
| Adverse Event Related to Progression | - |
| Consent withdrawn by subject | 2 |
| Other | 1 |
| Death | 41 |
| Sponsor Discontinued Study | 15 |
| Progressive Disease, Per Protocol | - |
| Lost to follow-up | 2 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Etoposide |
|-----------------------|---|

Reporting group description:

Participants received 80 mg veliparib orally twice a day (BID) on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered intravenously (IV) on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|--|
| Reporting group title | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Etoposide |
|-----------------------|--|

Reporting group description:

Participants received 120 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|--|
| Reporting group title | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Etoposide |
|-----------------------|--|

Reporting group description:

Participants received 160 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|--|
| Reporting group title | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Etoposide |
|-----------------------|--|

Reporting group description:

Participants received 200 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|--|
| Reporting group title | Phase 1: Veliparib 240 mg BID 7 Days + Carboplatin/Etoposide |
|-----------------------|--|

Reporting group description:

Participants received 240 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 1: Veliparib 240 mg BID 14 Days + Carboplatin/Etoposide |
|-----------------------|---|

Reporting group description:

Participants received 240 mg veliparib orally BID on Days -2 to 12 (14 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 12 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 1: Veliparib 240 mg BID 21 Days + Carboplatin/Etoposide |
|-----------------------|---|

Reporting group description:

Participants received 240 mg veliparib orally BID on Days -2 to Day 19 (continuous schedule) in combination with carboplatin/etoposide for up to four 21-day cycles. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 2: Veliparib + Carboplatin/Etoposide -> Veliparib |
|-----------------------|---|

Reporting group description:

Participants in Arm A received veliparib 240 mg BID on Day -2 to 12 (14-day schedule), carboplatin AUC 5 mg/mL*min administered on Day 1, and etoposide 100 mg/m² administered on Days 1 to 3 of each 21-day cycle for up to 6 cycles.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 2: Veliparib + Carboplatin/Etoposide -> Placebo |
|-----------------------|---|

Reporting group description:

Participants In Arm B received veliparib 240 mg BID on Day -2 to 12 (14-day schedule), carboplatin AUC 5 mg/mL*min administered on Day 1, and etoposide 100 mg/m² administered on Days 1 to 3 of each 21-day cycle for up to 6 cycles.

Participants without evidence of disease progression received placebo monotherapy BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 2: Placebo + Carboplatin/Etoposide -> Placebo |
|-----------------------|---|

Reporting group description:

Participants in Arm C received placebo BID on Day -2 to 12 (14-day schedule), carboplatin AUC 5 mg/mL*min on Day 1, and etoposide 100 mg/m² on Days 1 to 3 of each 21-day cycle for up to 6 cycles. Participants without evidence of disease progression received placebo monotherapy BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| Reporting group values | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Etoposide |
|------------------------------------|---|--|--|
| Number of subjects | 4 | 3 | 4 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|----------------------|----------------------|----------------------|
| Age continuous Units: years median full range (min-max) | 74.0 55.0 to 79.0 | 69.0 62.0 to 75.0 | 62.5 56.0 to 74.0 |
| Gender categorical Units: Subjects | | | |
| Female | 3 | 0 | 2 |
| Male | 1 | 3 | 2 |
| Race Units: Subjects | | | |
| White | 4 | 3 | 4 |
| Black or African American | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Missing | 0 | 0 | 0 |
| Eastern Cooperative Oncology Group (ECOG) Performance Status | | | |
| Measure Description: ECOG performance status is used by doctors and researchers to assess how a participant's disease is progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. 0 = Fully Active (Most Favorable Activity); | | | |

| | | | |
|--|---|---|---|
| 1 = Restricted activity but ambulatory; 2 = Ambulatory but unable to carry out work activities; 3 = Limited Self-Care; 4 = Completely Disabled, No self-care (Least Favorable Activity) | | | |
| Units: Subjects | | | |
| 0 - Fully active | 1 | 1 | 1 |
| 1 - Restricted but ambulatory | 3 | 2 | 3 |
| Missing | 0 | 0 | 0 |

| Reporting group values | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 240 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 240 mg BID 14 Days + Carboplatin/Etoposide |
|------------------------|---|---|--|
| Number of subjects | 3 | 8 | 14 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|--------------|--------------|--------------|
| Age continuous | | | |
| Units: years | | | |
| median | 54.0 | 52.0 | 66.0 |
| full range (min-max) | 52.0 to 68.0 | 43.0 to 63.0 | 52.0 to 72.0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 1 | 2 | 5 |
| Male | 2 | 6 | 9 |
| Race | | | |
| Units: Subjects | | | |
| White | 3 | 8 | 14 |
| Black or African American | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Missing | 0 | 0 | 0 |
| Eastern Cooperative Oncology Group (ECOG) Performance Status | | | |
| Measure Description: ECOG performance status is used by doctors and researchers to assess how a participant's disease is progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. 0 = Fully Active (Most Favorable Activity); 1 = Restricted activity but ambulatory; 2 = Ambulatory but unable to carry out work activities; 3 = Limited Self-Care; 4 = Completely Disabled, No self-care (Least Favorable Activity) | | | |
| Units: Subjects | | | |
| 0 - Fully active | 1 | 2 | 3 |
| 1 - Restricted but ambulatory | 2 | 5 | 11 |
| Missing | 0 | 1 | 0 |

| Reporting group values | Phase 1: Veliparib 240 mg BID 21 Days + Carboplatin/Etoposide | Phase 2: Veliparib + Carboplatin/Etoposide -> Veliparib | Phase 2: Veliparib + Carboplatin/Etoposide -> Placebo |
|------------------------|--|---|---|
| Number of subjects | 4 | 61 | 59 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|----------------------|----------------------|----------------------|
| Age continuous Units: years median full range (min-max) | 59.0 57.0 to 62.0 | 62.0 39.0 to 77.0 | 64.0 46.0 to 86.0 |
| Gender categorical Units: Subjects | | | |
| Female | 1 | 21 | 21 |
| Male | 3 | 40 | 38 |
| Race Units: Subjects | | | |
| White | 4 | 55 | 51 |
| Black or African American | 0 | 2 | 1 |
| Asian | 0 | 4 | 7 |
| Missing | 0 | 0 | 0 |
| Eastern Cooperative Oncology Group (ECOG) Performance Status | | | |
| Measure Description: ECOG performance status is used by doctors and researchers to assess how a participant's disease is progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. 0 = Fully Active (Most Favorable Activity); 1 = Restricted activity but ambulatory; 2 = Ambulatory but unable to carry out work activities; 3 = Limited Self-Care; 4 = Completely Disabled, No self-care (Least Favorable Activity) | | | |
| Units: Subjects | | | |
| 0 - Fully active | 2 | 21 | 16 |
| 1 - Restricted but ambulatory | 1 | 39 | 42 |
| Missing | 1 | 1 | 1 |

| | | | |
|------------------------------------|---|-------|--|
| Reporting group values | Phase 2: Placebo + Carboplatin/Etoposide -> Placebo | Total | |
| Number of subjects | 61 | 221 | |
| Age categorical Units: Subjects | | | |

| | | | |
|--|----------------------|-----|--|
| Age continuous Units: years median full range (min-max) | 63.0 37.0 to 87.0 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 23 | 79 | |
| Male | 38 | 142 | |
| Race Units: Subjects | | | |
| White | 52 | 198 | |
| Black or African American | 1 | 4 | |
| Asian | 7 | 18 | |
| Missing | 1 | 1 | |
| Eastern Cooperative Oncology Group (ECOG) Performance Status | | | |
| Measure Description: ECOG performance status is used by doctors and researchers to assess how a participant's disease is progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. | | | |

| | | | |
|---|----|-----|--|
| 0 = Fully Active (Most Favorable Activity); 1 = Restricted activity but ambulatory; 2 = Ambulatory but unable to carry out work activities; 3 = Limited Self-Care; 4 = Completely Disabled, No self-care (Least Favorable Activity) | | | |
| Units: Subjects | | | |
| 0 - Fully active | 23 | 71 | |
| 1 - Restricted but ambulatory | 37 | 145 | |
| Missing | 1 | 5 | |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Etoposide |
| Reporting group description: Participants received 80 mg veliparib orally twice a day (BID) on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered intravenously (IV) on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m ² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity. | |
| Reporting group title | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Etoposide |
| Reporting group description: Participants received 120 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m ² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity. | |
| Reporting group title | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Etoposide |
| Reporting group description: Participants received 160 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m ² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity. | |
| Reporting group title | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Etoposide |
| Reporting group description: Participants received 200 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m ² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity. | |
| Reporting group title | Phase 1: Veliparib 240 mg BID 7 Days + Carboplatin/Etoposide |
| Reporting group description: Participants received 240 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m ² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity. | |
| Reporting group title | Phase 1: Veliparib 240 mg BID 14 Days + Carboplatin/Etoposide |
| Reporting group description: Participants received 240 mg veliparib orally BID on Days -2 to 12 (14 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 12 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m ² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity. | |
| Reporting group title | Phase 1: Veliparib 240 mg BID 21 Days + Carboplatin/Etoposide |

Reporting group description:

Participants received 240 mg veliparib orally BID on Days -2 to Day 19 (continuous schedule) in combination with carboplatin/etoposide for up to four 21-day cycles. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 2: Veliparib + Carboplatin/Etoposide -> Veliparib |
|-----------------------|---|

Reporting group description:

Participants in Arm A received veliparib 240 mg BID on Day -2 to 12 (14-day schedule), carboplatin AUC 5 mg/mL*min administered on Day 1, and etoposide 100 mg/m² administered on Days 1 to 3 of each 21-day cycle for up to 6 cycles.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 2: Veliparib + Carboplatin/Etoposide -> Placebo |
|-----------------------|---|

Reporting group description:

Participants In Arm B received veliparib 240 mg BID on Day -2 to 12 (14-day schedule), carboplatin AUC 5 mg/mL*min administered on Day 1, and etoposide 100 mg/m² administered on Days 1 to 3 of each 21-day cycle for up to 6 cycles.

Participants without evidence of disease progression received placebo monotherapy BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 2: Placebo + Carboplatin/Etoposide -> Placebo |
|-----------------------|---|

Reporting group description:

Participants in Arm C received placebo BID on Day -2 to 12 (14-day schedule), carboplatin AUC 5 mg/mL*min on Day 1, and etoposide 100 mg/m² on Days 1 to 3 of each 21-day cycle for up to 6 cycles.

Participants without evidence of disease progression received placebo monotherapy BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|----------------------------|--|
| Subject analysis set title | Phase 1: Veliparib 240 mg BID + Carboplatin/Etoposide Combined |
|----------------------------|--|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Participants received 240 mg veliparib orally BID (Days -2 to 5 for 7-day schedule, Days -2 to 12 for 14-day schedule or Days -2 to 19 for continuous dosing) in combination with carboplatin/etoposide for up to four 21-day cycles. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle.

| | |
|----------------------------|--|
| Subject analysis set title | Etoposide Cycle 1 Day 1 (With Veliparib) |
|----------------------------|--|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Phase 1 participants received 100 mg/m² etoposide intravenously with carboplatin target AUC 5.0 mg*min/mL and veliparib 80 to 240 mg BID on Cycle 1 Day 1.

| | |
|----------------------------|--|
| Subject analysis set title | Etoposide Cycle 2 Day 1 (No Veliparib) |
|----------------------------|--|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Phase 1 participants received etoposide 100 mg/m² and carboplatin target AUC 5.0 mg*min/mL on Day 1 of Cycle 2. No veliparib was administered.

Primary: Phase 1: Number of Participants With Dose-limiting Toxicities (DLTs)

| | |
|-----------------|--|
| End point title | Phase 1: Number of Participants With Dose-limiting Toxicities (DLTs) ^{[1][2]} |
|-----------------|--|

End point description:

A DLT was defined as any of the following drug-related toxicities, graded according to the Common Toxicity Criteria for Adverse Events (CTCAE), V.4.0:

1. Events associated with treatment delay >14 days in initiating Cycle 2 therapy:

Grade 4 thrombocytopenia, neutropenia, or febrile neutropenia, or Grade 3 febrile neutropenia with fever for > 7 days

2. Grade ≥ 3 non-hematologic toxicity with ≥ 2 grade increase from baseline and attributed to veliparib treatment, excluding nausea or vomiting for ≤ 48 hours or inadequately treated, electrolyte abnormalities resolving in ≤ 24 hours, hypersensitivity reactions or alopecia

3. Grade 2 non-hematologic toxicity of ≥ 2 grade increase from baseline, attributed to veliparib treatment requiring delay of >14 days in initiation of Cycle 2

4. Any toxicity of ≥ 2-grade increase from baseline, attributed to veliparib and requiring a dose

modification in Cycle 1 or omission of carboplatin, >1 daily etoposide dose, or >30% veliparib doses in Cycle 1

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

End point timeframe:

Cycle 1 Day -2 to pre-dose on Cycle 2 Day 1 (23 days)

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: Safety results were analyzed descriptively.

[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: Endpoint pertains to Phase 1 only.

| End point values | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Eto poside |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 3 | 4 | 3 |
| Units: participants | 0 | 0 | 0 | 0 |

| End point values | Phase 1: Veliparib 240 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 240 mg BID 14 Days + Carboplatin/Eto poside | Phase 1: Veliparib 240 mg BID 21 Days + Carboplatin/Eto poside | |
|-----------------------------|--|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 8 | 14 | 4 | |
| Units: participants | 1 | 0 | 1 | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Maximum Observed Plasma Concentration (Cmax) of Veliparib

| | |
|-----------------|--|
| End point title | Phase 1: Maximum Observed Plasma Concentration (Cmax) of Veliparib ^{[3][4]} |
|-----------------|--|

End point description:

Plasma concentrations of veliparib were determined using a validated online solid-phase extraction followed by high-performance liquid chromatography with tandem mass spectrometric detection (HPLC LC-MS/MS). The lower limit of quantitation (LLOQ) for veliparib was established at ≥ 1.05 ng/mL. The number of participants analyzed includes participants who were administered at least 1 dose of study drug, had at least 1 reported PK sample concentration and for whom Cmax could be calculated.

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

End point timeframe:

Cycle 1 Day 1 predose and at 1, 2, 3, 5, 8, and 24 hours post-dose

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: Pharmacokinetics were analyzed descriptively.

[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: Endpoint pertains to Phase 1 only.

| End point values | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Eto poside |
|---|---|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 3 | 4 | 3 |
| Units: µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | 0.620 (± 17) | 1.00 (± 31) | 1.39 (± 29) | 1.44 (± 10) |

| End point values | Phase 1: Veliparib 240 mg BID + Carboplatin/Eto poside Combined | | | |
|---|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 22 | | | |
| Units: µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | 1.99 (± 25) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Time to Maximum Observed Plasma Concentration (Tmax) of Veliparib

| | |
|-----------------|--|
| End point title | Phase 1: Time to Maximum Observed Plasma Concentration (Tmax) of Veliparib ^{[5][6]} |
|-----------------|--|

End point description:

Plasma concentrations of veliparib were determined using a validated online solid-phase extraction followed by high-performance liquid chromatography with tandem mass spectrometric detection (HPLC LC-MS/MS). The lower limit of quantitation (LLOQ) for veliparib was established at ≥ 1.05 ng/mL. The number of participants analyzed includes participants who were administered at least 1 dose of study drug, had at least 1 reported PK sample concentration and for whom Tmax could be calculated.

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

End point timeframe:

Cycle 1 Day 1 predose and at 1, 2, 3, 5, 8, and 24 hours post-dose

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: Pharmacokinetics were analyzed descriptively.

[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: Endpoint pertains to Phase 1 only.

| End point values | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Eto poside |
|-------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 3 | 4 | 3 |
| Units: hours | | | | |
| median (full range (min-max)) | 2.0 (1.0 to 2.0) | 1.0 (1.0 to 2.0) | 1.5 (1.0 to 2.0) | 2.0 (1.0 to 2.0) |

| End point values | Phase 1: Veliparib 240 mg BID + Carboplatin/Eto poside Combined | | | |
|-------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 22 | | | |
| Units: hours | | | | |
| median (full range (min-max)) | 1.0 (1.0 to 3.0) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Area Under the Plasma Concentration-time Curve From Time 0 to 8 Hours Post-dose (AUC[0-8]) of Veliparib

| | |
|-----------------|--|
| End point title | Phase 1: Area Under the Plasma Concentration-time Curve From Time 0 to 8 Hours Post-dose (AUC[0-8]) of Veliparib ^{[7][8]} |
|-----------------|--|

End point description:

The area under the plasma concentration-time curve from time 0 to 8 hours post-dose for veliparib was estimated using non-compartmental methods.

The number of participants analyzed includes participants who were administered at least 1 dose of study drug, had at least 1 reported PK sample concentration and for whom AUC(0-8) could be calculated.

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

End point timeframe:

Cycle 1 Day 1 predose and at 1, 2, 3, 5, 8, and 24 hours post-dose

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: Pharmacokinetics were analyzed descriptively.

[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: Endpoint pertains to Phase 1 only.

| End point values | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Eto poside |
|---|---|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 3 | 4 | 2 |
| Units: µg*h/mL | | | | |
| geometric mean (geometric coefficient of variation) | 3.18 (± 14) | 4.24 (± 25) | 7.51 (± 28) | 6.66 (± 4) |

| End point values | Phase 1: Veliparib 240 mg BID + Carboplatin/Eto poside Combined | | | |
|---|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 22 | | | |
| Units: µg*h/mL | | | | |
| geometric mean (geometric coefficient of variation) | 9.29 (± 37) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Area Under the Plasma Concentration-time Curve From Time 0 to 12 Hours Post-dose (AUC[0-12]) of Veliparib

| | |
|-----------------|---|
| End point title | Phase 1: Area Under the Plasma Concentration-time Curve From Time 0 to 12 Hours Post-dose (AUC[0-12]) of Veliparib ^{[9][10]} |
|-----------------|---|

End point description:

The area under the plasma concentration-time curve from time 0 to 12 hours post-dose for veliparib was estimated

using non-compartmental methods. AUC(0-12) was calculated by assuming the concentration at 12 hours post-dose

was the same as the pre-dose concentration.

The number of participants analyzed includes participants who were administered at least 1 dose of study drug, had at least 1 reported PK sample concentration and for whom AUC(0-12) could be calculated.

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

End point timeframe:

Cycle 1 Day 1 predose and at 1, 2, 3, 5, 8, and 24 hours post-dose

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: Pharmacokinetics were analyzed descriptively.

[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: Endpoint pertains to Phase 1 only.

| End point values | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Eto poside |
|---|---|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 3 | 4 | 3 |
| Units: µg*h/mL | | | | |
| geometric mean (geometric coefficient of variation) | 4.07 (± 15) | 5.25 (± 27) | 9.71 (± 31) | 8.35 (± 6) |

| End point values | Phase 1: Veliparib 240 mg BID + Carboplatin/Eto poside Combined | | | |
|---|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 22 | | | |
| Units: µg*h/mL | | | | |
| geometric mean (geometric coefficient of variation) | 11.6 (± 40) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Dose-normalized Maximum Observed Plasma Concentration of Veliparib

| | |
|-----------------|---|
| End point title | Phase 1: Dose-normalized Maximum Observed Plasma Concentration of Veliparib ^{[11][12]} |
|-----------------|---|

End point description:

Plasma concentrations of veliparib were determined using a validated online solid-phase extraction followed by high-performance liquid chromatography with tandem mass spectrometric detection (HPLC LC-MS/MS). The lower limit of quantitation (LLOQ) for veliparib was established at ≥ 1.05 ng/mL.

Dose normalized C_{max} is calculated as C_{max} / veliparib dose in mg.

The number of participants analyzed includes participants who were administered at least 1 dose of study drug, had at least 1 reported PK sample concentration and for whom C_{max} could be calculated.

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

End point timeframe:

Cycle 1 Day 1 predose and at 1, 2, 3, 5, 8, and 24 hours post-dose

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: Pharmacokinetics were analyzed descriptively.

[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: Endpoint pertains to Phase 1 only.

| End point values | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Eto poside |
|---|---|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 3 | 4 | 3 |
| Units: (ng/mL)/mg | | | | |
| geometric mean (geometric coefficient of variation) | 7.75 (± 16) | 8.35 (± 31) | 8.66 (± 29) | 7.19 (± 10) |

| End point values | Phase 1: Veliparib 240 mg BID + Carboplatin/Eto poside Combined | | | |
|---|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 22 | | | |
| Units: (ng/mL)/mg | | | | |
| geometric mean (geometric coefficient of variation) | 8.31 (± 25) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Dose-normalized Area Under the Plasma Concentration-time Curve From Time 0 to 8 Hours Post-dose of Veliparib

| | |
|-----------------|---|
| End point title | Phase 1: Dose-normalized Area Under the Plasma Concentration-time Curve From Time 0 to 8 Hours Post-dose of Veliparib ^[13] ^[14] |
|-----------------|---|

End point description:

The area under the plasma concentration-time curve from time 0 to 8 hours post-dose for veliparib was estimated using non-compartmental methods.

Dose normalized AUC(0-8) is calculated as AUC(0-8) / veliparib dose in mg.

The number of participants analyzed includes participants who were administered at least 1 dose of study drug, had at least 1 reported PK sample concentration and for whom AUC(0-8) could be calculated.

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

End point timeframe:

Cycle 1 Day 1 predose and at 1, 2, 3, 5, 8, and 24 hours post-dose

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: Pharmacokinetics were analyzed descriptively.

[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: Endpoint pertains to Phase 1 only.

| End point values | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Eto poside |
|---|---|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 3 | 4 | 2 |
| Units: (ng*h/mL)/mg | | | | |
| geometric mean (geometric coefficient of variation) | 39.8 (± 14) | 35.3 (± 25) | 46.9 (± 28) | 33.3 (± 4) |

| End point values | Phase 1: Veliparib 240 mg BID + Carboplatin/Eto poside Combined | | | |
|---|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 22 | | | |
| Units: (ng*h/mL)/mg | | | | |
| geometric mean (geometric coefficient of variation) | 38.7 (± 37) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Dose-normalized Area Under the Plasma Concentration-time Curve From Time 0 to 12 Hours Post-dose of Veliparib

| | |
|-----------------|--|
| End point title | Phase 1: Dose-normalized Area Under the Plasma Concentration-time Curve From Time 0 to 12 Hours Post-dose of Veliparib ^{[15][16]} |
|-----------------|--|

End point description:

The area under the plasma concentration-time curve from time 0 to 12 hours post-dose for veliparib was estimated using non-compartmental methods. AUC(0-12) was calculated by assuming the concentration at 12 hours post-dose was the same as the pre-dose concentration. Dose normalized AUC(0-12) is calculated as AUC(0-12) / veliparib dose in mg.

The number of participants analyzed includes participants who were administered at least 1 dose of study drug, had at least 1 reported PK sample concentration and for whom AUC(0-12) could be calculated.

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

End point timeframe:

Cycle 1 Day 1 predose and at 1, 2, 3, 5, 8, and 24 hours post-dose

Notes:

[15] - 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: Pharmacokinetics were analyzed descriptively.

[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: Endpoint pertains to Phase 1 only.

| End point values | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Eto poside |
|---|---|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 3 | 4 | 3 |
| Units: (ng*h/mL)/mg | | | | |
| geometric mean (geometric coefficient of variation) | 50.9 (± 15) | 43.8 (± 27) | 60.7 (± 31) | 41.7 (± 6) |

| End point values | Phase 1: Veliparib 240 mg BID + Carboplatin/Eto poside Combined | | | |
|---|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 22 | | | |
| Units: (ng*h/mL)/mg | | | | |
| geometric mean (geometric coefficient of variation) | 48.5 (± 40) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Maximum Observed Plasma Concentration (Cmax) of Etoposide With and Without Veliparib

| | |
|-----------------|---|
| End point title | Phase 1: Maximum Observed Plasma Concentration (Cmax) of Etoposide With and Without Veliparib ^[17] |
|-----------------|---|

End point description:

Etoposide plasma concentrations were determined using liquid chromatography with tandem mass spectrometric detection with a lower limit of quantitation 160 ng/mL.

The number of participants analyzed includes participants who received at least 1 dose of study drug, had at least 1 reported PK sample concentration for each time point and for whom Cmax could be calculated. Participants in the Veliparib 240 mg BID 21-day (continuous) dosing group and participants whose etoposide dose was reduced in Cycle 2 are not included in the Cycle 2 Day 1 analysis.

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

End point timeframe:

Cycle 1 Day 1 (coadministered with veliparib and carboplatin), and on Cycle 2 Day 1 (co-administered with carboplatin but in the absence of veliparib) at 55 minutes (5 minutes before the end of infusion) and 3, 5, 8, and 24 hours post-dose.

Notes:

[17] - 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: Pharmacokinetics were analyzed descriptively.

| End point values | Etoposide Cycle 1 Day 1 (With Veliparib) | Etoposide Cycle 2 Day 1 (No Veliparib) | | |
|---|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 37 | 23 | | |
| Units: µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | 16.9 (± 18) | 16.4 (± 21) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Time to Maximum Observed Plasma Concentration (Tmax) of Etoposide With and Without Veliparib

| | |
|-----------------|---|
| End point title | Phase 1: Time to Maximum Observed Plasma Concentration (Tmax) of Etoposide With and Without Veliparib ^[18] |
|-----------------|---|

End point description:

Etoposide plasma concentrations were determined using liquid chromatography with tandem mass spectrometric detection with a lower limit of quantitation 160 ng/mL. The number of participants analyzed includes participants who received at least 1 dose of study drug, had at least 1 reported PK sample concentration for each time point and for whom Tmax could be calculated. Participants in the Veliparib 240 mg BID 21-day (continuous) dosing group are not included in the Cycle 2 Day 1 analysis.

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

End point timeframe:

Cycle 1 Day 1 (coadministered with veliparib and carboplatin), and on Cycle 2 Day 1 (co-administered with carboplatin but in the absence of veliparib) at 55 minutes (5 minutes before the end of infusion) and 3, 5, 8, and 24 hours post-dose.

Notes:

[18] - 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: Pharmacokinetics were analyzed descriptively.

| End point values | Etoposide Cycle 1 Day 1 (With Veliparib) | Etoposide Cycle 2 Day 1 (No Veliparib) | | |
|-------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 37 | 28 | | |
| Units: hours | | | | |
| median (full range (min-max)) | 0.9 (0.8 to 3.0) | 0.9 (0.9 to 3.7) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Area Under the Concentration-time Curve From Time 0 to Time of Last Measurable Concentration (AUC[0-t]) of Etoposide With and Without Veliparib

| | |
|-----------------|---|
| End point title | Phase 1: Area Under the Concentration-time Curve From Time 0 to Time of Last Measurable Concentration (AUC[0-t]) of |
|-----------------|---|

End point description:

The area under the plasma concentration-time curve from 0 to the last measurable concentration (24 hours) of

etoposide was estimated using non-compartmental methods.

The number of participants analyzed includes participants who received at least 1 dose of study drug, had at least 1 reported PK sample concentration for each time point and for whom AUC(0-t) could be calculated. Participants in the Veliparib 240 mg BID 21-day (continuous) dosing group and participants whose etoposide dose was reduced in Cycle 2 are not included in the Cycle 2 Day 1 analysis.

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

End point timeframe:

Cycle 1 Day 1 (coadministered with veliparib and carboplatin), and on Cycle 2 Day 1 (co-administered with carboplatin but in the absence of veliparib) at 55 minutes (5 minutes before the end of infusion) and 3, 5, 8, and 24 hours post-dose.

Notes:

[19] - 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: Pharmacokinetics were analyzed descriptively.

| End point values | Etoposide Cycle 1 Day 1 (With Veliparib) | Etoposide Cycle 2 Day 1 (No Veliparib) | | |
|---|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 35 | 22 | | |
| Units: µg*h/mL | | | | |
| geometric mean (geometric coefficient of variation) | 102 (± 23) | 94.7 (± 18) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Area Under the Concentration-time Curve From Time 0 to Infinity (AUC[0-∞]) of Etoposide With and Without Veliparib

| | |
|-----------------|---|
| End point title | Phase 1: Area Under the Concentration-time Curve From Time 0 to Infinity (AUC[0-∞]) of Etoposide With and Without Veliparib ^[20] |
|-----------------|---|

End point description:

The area under the plasma concentration-time curve from 0 to infinity for etoposide was estimated using non-compartmental methods.

The number of participants analyzed includes participants who received at least 1 dose of study drug, had at least 1 reported PK sample concentration for each time point and for whom AUC(0-∞) could be calculated. Participants in the Veliparib 240 mg BID 21-day (continuous) dosing group and participants whose etoposide dose was reduced in Cycle 2 are not included in the Cycle 2 Day 1 analysis.

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

End point timeframe:

Cycle 1 Day 1 (coadministered with veliparib and carboplatin), and on Cycle 2 Day 1 (co-administered with carboplatin but in the absence of veliparib) at 55 minutes (5 minutes before the end of infusion) and 3, 5, 8, and 24 hours post-dose.

Notes:

[20] - 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: Pharmacokinetics were analyzed descriptively.

| End point values | Etoposide Cycle 1 Day 1 (With Veliparib) | Etoposide Cycle 2 Day 1 (No Veliparib) | | |
|---|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 35 | 22 | | |
| Units: µg*h/m | | | | |
| geometric mean (geometric coefficient of variation) | 112 (± 56) | 99.5 (± 18) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Terminal Phase Elimination Half-life (t_{1/2}) of Etoposide With and Without Veliparib

| | |
|-----------------|---|
| End point title | Phase 1: Terminal Phase Elimination Half-life (t _{1/2}) of Etoposide With and Without Veliparib ^[21] |
|-----------------|---|

End point description:

The terminal half-life of etoposide was estimated using non-compartmental methods. Values reported represent the harmonic mean ± pseudo-standard deviation. The number of participants analyzed includes participants who received at least 1 dose of study drug, had at least 1 reported PK sample concentration for each time point and for whom t_{1/2} could be calculated. Participants in the Veliparib 240 mg BID 21-day (continuous) dosing group are not included in the Cycle 2 Day 1 analysis.

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

End point timeframe:

Cycle 1 Day 1 (coadministered with veliparib and carboplatin), and on Cycle 2 Day 1 (co-administered with carboplatin but in the absence of veliparib) at 55 minutes (5 minutes before the end of infusion) and 3, 5, 8, and 24 hours post-dose.

Notes:

[21] - 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: Pharmacokinetics were analyzed descriptively.

| End point values | Etoposide Cycle 1 Day 1 (With Veliparib) | Etoposide Cycle 2 Day 1 (No Veliparib) | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 35 | 27 | | |
| Units: hours | | | | |
| arithmetic mean (standard deviation) | 5.7 (± 1.5) | 5.0 (± 1.2) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Dose-normalized Maximum Observed Plasma Concentration (C_{max}) of Etoposide With and Without Veliparib

| | |
|-----------------|--|
| End point title | Phase 1: Dose-normalized Maximum Observed Plasma Concentration (C _{max}) of Etoposide With and Without Veliparib |
|-----------------|--|

End point description:

Etoposide plasma concentrations were determined using liquid chromatography with tandem mass spectrometric detection with a lower limit of quantitation 160 ng/mL. Dose normalized C_{max} is calculated as C_{max} / etoposide dose in mg/m².

The number of participants analyzed includes participants who received at least 1 dose of study drug, had at least 1 reported PK sample concentration for each time point and for whom C_{max} could be calculated. Participants in the Veliparib 240 mg BID 21-day (continuous) dosing group are not included in the Cycle 2 Day 1 analysis.

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

End point timeframe:

Cycle 1 Day 1 (coadministered with veliparib and carboplatin), and on Cycle 2 Day 1 (co-administered with carboplatin but in the absence of veliparib) at 55 minutes (5 minutes before the end of infusion) and 3, 5, 8, and 24 hours post-dose.

Notes:

[22] - 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: Pharmacokinetics were analyzed descriptively.

| End point values | Etoposide Cycle 1 Day 1 (With Veliparib) | Etoposide Cycle 2 Day 1 (No Veliparib) | | |
|---|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 37 | 28 | | |
| Units: (ng/mL)/(mg/m ²) | | | | |
| geometric mean (geometric coefficient of variation) | 169 (± 18) | 170 (± 20) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Dose-normalized Area Under the Concentration-time Curve From Time 0 to Time of Last Measurable Concentration (AUC[0-t]) of Etoposide With and Without Veliparib

| | |
|-----------------|--|
| End point title | Phase 1: Dose-normalized Area Under the Concentration-time Curve From Time 0 to Time of Last Measurable Concentration (AUC[0-t]) of Etoposide With and Without Veliparib ^[23] |
|-----------------|--|

End point description:

The area under the plasma concentration-time curve from 0 to the last measurable concentration (24 hours) of

etoposide was estimated using non-compartmental methods. Dose normalized AUC(0-t) is calculated as AUC(0-t) / etoposide dose in mg/m².

The number of participants analyzed includes participants who received at least 1 dose of study drug, had at least 1 reported PK sample concentration for each time point and for whom AUC(0-t) could be calculated. Participants in the Veliparib 240 mg BID 21-day (continuous) dosing group are not included in the Cycle 2 Day 1 analysis.

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

End point timeframe:

Cycle 1 Day 1 (coadministered with veliparib and carboplatin), and on Cycle 2 Day 1 (co-administered with carboplatin but in the absence of veliparib) at 55 minutes (5 minutes before the end of infusion) and 3, 5, 8, and 24 hours post-dose.

Notes:

[23] - 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: Pharmacokinetics were analyzed descriptively.

| End point values | Etoposide Cycle 1 Day 1 (With Veliparib) | Etoposide Cycle 2 Day 1 (No Veliparib) | | |
|---|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 35 | 27 | | |
| Units: (ng*h/mL)/(mg/m ²) | | | | |
| geometric mean (geometric coefficient of variation) | 1020 (± 23) | 952 (± 21) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Dose-normalized Area Under the Concentration-time Curve From Time 0 to Infinity (AUC[0-∞]) of Etoposide With and Without Veliparib

| | |
|-----------------|---|
| End point title | Phase 1: Dose-normalized Area Under the Concentration-time Curve From Time 0 to Infinity (AUC[0-∞]) of Etoposide With and Without Veliparib ^[24] |
|-----------------|---|

End point description:

The area under the plasma concentration-time curve from 0 to infinity for etoposide was estimated using non-compartmental methods. Dose normalized AUC(0-∞) is calculated as AUC(0-∞) / etoposide dose in mg/m².

The number of participants analyzed includes participants who received at least 1 dose of study drug, had at least 1 reported PK sample concentration for each time point and for whom AUC(0-∞) could be calculated. Participants in the Veliparib 240 mg BID 21-day (continuous) dosing group are not included in the Cycle 2 Day 1 analysis.

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

End point timeframe:

Cycle 1 Day 1 (coadministered with veliparib and carboplatin), and on Cycle 2 Day 1 (co-administered with carboplatin but in the absence of veliparib) at 55 minutes (5 minutes before the end of infusion) and 3, 5, 8, and 24 hours post-dose.

Notes:

[24] - 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: Pharmacokinetics were analyzed descriptively.

| End point values | Etoposide Cycle 1 Day 1 (With Veliparib) | Etoposide Cycle 2 Day 1 (No Veliparib) | | |
|---|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 35 | 27 | | |
| Units: ng*h/mL)/(mg/m ²) | | | | |
| geometric mean (geometric coefficient of variation) | 1120 (± 56) | 1020 (± 20) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Progression-free Survival

| | |
|--|--|
| End point title | Phase 2: Progression-free Survival ^[25] |
| End point description: | |
| <p>Progression-free survival (PFS) is defined as the time from the date of randomization to the date of earliest radiographic disease progression or death if no radiographic disease progression occurred. If a participant did not have an event of disease progression and had not died on or prior to the cutoff for PFS analysis, the participant was censored at the date of their last disease assessment or randomization date provided they did not have any post-baseline disease assessment. Disease assessments were performed using computed tomography according to Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1.</p> <p>Progressive Disease (PD) was defined as at least a 20% increase in the size of target lesions and an absolute increase of at least 5 mm taking as reference the smallest lesion size recorded since the treatment started (baseline or after), or the appearance of 1 or more new lesions.</p> <p>The number of participants analyzed includes all participants randomized in Phase 2.</p> | |
| End point type | Primary |
| End point timeframe: | |
| From randomization up to the date the 126th PFS event was reached; Median time on follow-up was 7.3, 7.1, and 8.9 months in each treatment group respectively. | |
| 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: Endpoint pertains to Phase 2 only. | |

| End point values | Phase 2: Veliparib + Carboplatin/Eto poside -> Veliparib | Phase 2: Veliparib + Carboplatin/Eto poside -> Placebo | Phase 2: Placebo + Carboplatin/Eto poside -> Placebo | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 61 | 59 | 61 | |
| Units: months | | | | |
| median (confidence interval 80%) | 5.8 (5.6 to 6.8) | 5.7 (5.6 to 5.8) | 5.6 (5.1 to 6.7) | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Primary Analysis of PFS (Arm A vs. Arm C) |
| Statistical analysis description: | |
| <p>The primary efficacy analysis in the Phase 2 portion of the study was the comparison of PFS among participants who received veliparib in combination with carboplatin and etoposide followed by veliparib maintenance monotherapy (Arm A) vs. placebo in combination with carboplatin and etoposide followed by placebo maintenance monotherapy (Arm C).</p> <p>The hazard ratio was estimated from a Cox proportional hazards model stratified by lactate dehydrogenase (LDH) level. A hazard ratio < 1 favors Arm A.</p> | |
| Comparison groups | Phase 2: Veliparib + Carboplatin/Etoposide -> Veliparib v Phase 2: Placebo + Carboplatin/Etoposide -> Placebo |
| Number of subjects included in analysis | 122 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[26] |
| P-value | = 0.059 ^[27] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.665 |

| | |
|---------------------|-------------|
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 0.503 |
| upper limit | 0.88 |

Notes:

[26] - Statistical significance was determined by a two-sided p-value ≤ 0.2 .

[27] - Two-sided log-rank test stratified by lactate dehydrogenase (LDH) level.

| | |
|-----------------------------------|---|
| Statistical analysis title | Secondary Analysis of PFS (Arm B vs. Arm C) |
|-----------------------------------|---|

Statistical analysis description:

The analysis of PFS between Arm B versus Arm C was considered a secondary endpoint in the testing hierarchy (see details below), and was compared using a two-sided log-rank test stratified by LDH level. The hazard ratio was estimated from a Cox proportional hazards model stratified by LDH level. A hazard ratio of < 1 favors Arm B.

| | |
|---|---|
| Comparison groups | Phase 2: Placebo + Carboplatin/Etoposide -> Placebo v Phase 2: Veliparib + Carboplatin/Etoposide -> Placebo |
| Number of subjects included in analysis | 120 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[28] |
| P-value | = 0.924 ^[29] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.979 |

| | |
|---------------------|-------------|
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 0.744 |
| upper limit | 1.288 |

Notes:

[28] - If the primary analysis of PFS (Arm A vs Arm C) was statistically significant a fixed sequence testing procedure was to be performed with a 2-sided significance level of 0.2 for the following key secondary endpoints:

OS (Arm A vs Arm C)

PFS (Arms B vs Arm C)

OS (Arm B vs Arm C)

ORR (Arm A vs Arm C)

ORR (Arm B vs Arm C)

If significance versus Arm C was not demonstrated, all endpoints later in the testing hierarchy were to be considered exploratory.

[29] - Two-sided log-rank test stratified by lactate dehydrogenase (LDH) level.

Secondary: Phase 2: Overall Survival

| | |
|-----------------|---|
| End point title | Phase 2: Overall Survival ^[30] |
|-----------------|---|

End point description:

Overall survival (OS) is defined as the time from the date of randomization to the date of death. If a participant did not die on or prior to the end of study, the participant was censored at the date of their last known alive date, which is defined as the last date of the last survival follow-up visit, the start date of the last adverse event (AE), the start date or end date of the last dose of any study drugs, the last lab and vital sign collection date, or the last disease assessment date, whichever occurred last.

The number of participants analyzed includes all participants randomized in Phase 2.

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

End point timeframe:

From randomization until the end of study (after a total of 136 OS events); median time on follow-up was 10.0, 8.6, and 11.7 months in each treatment group respectively.

Notes:

[30] - 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: Endpoint pertains to Phase 2 only.

| End point values | Phase 2: Veliparib + Carboplatin/Eto poside -> Veliparib | Phase 2: Veliparib + Carboplatin/Eto poside -> Placebo | Phase 2: Placebo + Carboplatin/Eto poside -> Placebo | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 61 | 59 | 61 | |
| Units: months | | | | |
| median (confidence interval 80%) | 10.1 (9.2 to 11.4) | 10.0 (8.0 to 12.7) | 12.4 (11.1 to 13.6) | |

Statistical analyses

| Statistical analysis title | Overall Survival of Arm A vs. Arm C |
|--|--|
| Statistical analysis description: | |
| The analysis of OS between Arm A versus Arm C was a key secondary endpoint in the testing hierarchy (see details below), and was compared using a two-sided log-rank test stratified by LDH level. The hazard ratio was estimated from a Cox proportional hazards model stratified by LDH level. A hazard ratio of < 1 favors Arm A. | |
| Comparison groups | Phase 2: Veliparib + Carboplatin/Etoposide -> Veliparib v Phase 2: Placebo + Carboplatin/Etoposide -> Placebo |
| Number of subjects included in analysis | 122 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[31] |
| P-value | = 0.088 ^[32] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.432 |
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 1.092 |
| upper limit | 1.879 |

Notes:

[31] - If the primary analysis of PFS (Arm A vs Arm C) was statistically significant a fixed sequence testing procedure was to be performed with a 2-sided significance level of 0.2 for the following key secondary endpoints:

OS (Arm A vs Arm C)

PFS (Arms B vs Arm C)

OS (Arm B vs Arm C)

ORR (Arm A vs Arm C)

ORR (Arm B vs Arm C)

If significance versus Arm C was not demonstrated, all endpoints later in the testing hierarchy were to be considered exploratory.

[32] - Two-sided log rank test stratified by LDH level.

| Statistical analysis title | Overall Survival of Arm B vs. Arm C |
|----------------------------|-------------------------------------|
|----------------------------|-------------------------------------|

Statistical analysis description:

The analysis of OS between Arm B versus Arm C was a key secondary endpoint in the testing hierarchy (see details below), and was compared using a two-sided log-rank test stratified by LDH level.

The hazard ratio was estimated from a Cox proportional hazards model stratified by LDH level. A hazard ratio of < 1 favors Arm B.

| | |
|---|---|
| Comparison groups | Phase 2: Placebo + Carboplatin/Etoposide -> Placebo v Phase 2: Veliparib + Carboplatin/Etoposide -> Placebo |
| Number of subjects included in analysis | 120 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[33] |
| P-value | = 0.083 ^[34] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.46 |
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 1.104 |
| upper limit | 1.931 |

Notes:

[33] - If the primary analysis of PFS (Arm A vs Arm C) was statistically significant a fixed sequence testing procedure was to be performed with a 2-sided significance level of 0.2 for the following key secondary endpoints:

OS (Arm A vs Arm C)

PFS (Arms B vs Arm C)

OS (Arm B vs Arm C)

ORR (Arm A vs Arm C)

ORR (Arm B vs Arm C)

If significance versus Arm C was not demonstrated, all endpoints later in the testing hierarchy were to be considered exploratory.

[34] - Two-sided log rank test stratified by LDH level.

Secondary: Phase 2: Objective Response Rate

| | |
|---|--|
| End point title | Phase 2: Objective Response Rate ^[35] |
| End point description: | |
| Objective response rate (ORR) is defined as the percentage of participants with objective response (confirmed) as assessed by the investigator using RECIST version 1.1. Objective response includes both complete response (CR) and partial response (PR). Response must be confirmed at a subsequent tumor assessment at least 28 days apart. Participants with no post-baseline confirmed response were counted as non-responders. | |
| CR: Disappearance of all target and non-target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. No new lesions. | |
| PR: At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters, and no new lesions. | |
| The number of participants analyzed includes all participants randomized in Phase 2. | |
| End point type | Secondary |

End point timeframe:

Tumor assessments were performed every 6 weeks for the first 30 weeks and every 9 weeks thereafter until disease progression; median time on follow-up was 7.3, 7.1, and 8.9 months in each group respectively.

Notes:

[35] - 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: Endpoint pertains to Phase 2 only.

| End point values | Phase 2: Veliparib + Carboplatin/Eto poside -> Veliparib | Phase 2: Veliparib + Carboplatin/Eto poside -> Placebo | Phase 2: Placebo + Carboplatin/Eto poside -> Placebo | |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 61 | 59 | 61 | |
| Units: percentage of participants | | | | |
| number (confidence interval 80%) | 77.0 (68.7 to 84.0) | 59.3 (50.1 to 68.0) | 63.9 (55.0 to 72.2) | |

Statistical analyses

| Statistical analysis title | Objective Response Rate of Arm A vs Arm C |
|--|--|
| Statistical analysis description: | |
| The analysis of ORR between Arm A versus Arm C was a key secondary endpoint in the testing hierarchy (see details below), and was compared using a two-sided Cochran-Mantel-Haenszel test stratified by LDH level. | |
| An odds ratio of > 1 favors Arm A. | |
| Comparison groups | Phase 2: Veliparib + Carboplatin/Etoposide -> Veliparib v Phase 2: Placebo + Carboplatin/Etoposide -> Placebo |
| Number of subjects included in analysis | 122 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[36] |
| P-value | = 0.115 ^[37] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.9 |
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 1.1 |
| upper limit | 3.2 |

Notes:

[36] - If the primary analysis of PFS (Arm A vs Arm C) was statistically significant a fixed sequence testing procedure was to be performed with a 2-sided significance level of 0.2 for the following key secondary endpoints:

OS (Arm A vs Arm C)
PFS (Arms B vs Arm C)
OS (Arm B vs Arm C)
ORR (Arm A vs Arm C)
ORR (Arm B vs Arm C)

If significance versus Arm C was not demonstrated, all endpoints later in the testing hierarchy were to be considered exploratory.

[37] - Cochran-Mantel-Haenszel test stratified by LDH level.

| Statistical analysis title | Objective Response Rate of Arm B vs Arm C |
|--|--|
| Statistical analysis description: | |
| The analysis of ORR between Arm B versus Arm C was a key secondary endpoint in the testing hierarchy (see details below), and was compared using a two-sided Cochran-Mantel-Haenszel test stratified by LDH level. | |
| An odds ratio of > 1 favors Arm B. | |
| Comparison groups | Phase 2: Placebo + Carboplatin/Etoposide -> Placebo v Phase 2: Veliparib + Carboplatin/Etoposide -> Placebo |

| | |
|---|-----------------------------|
| Number of subjects included in analysis | 120 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[38] |
| P-value | = 0.604 ^[39] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.8 |
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 1.3 |

Notes:

[38] - If the primary analysis of PFS (Arm A vs Arm C) was statistically significant a fixed sequence testing procedure was to be performed with a 2-sided significance level of 0.2 for the following key secondary endpoints:

OS (Arm A vs Arm C)

PFS (Arms B vs Arm C)

OS (Arm B vs Arm C)

ORR (Arm A vs Arm C)

ORR (Arm B vs Arm C)

If significance versus Arm C was not demonstrated, all endpoints later in the testing hierarchy were to be considered exploratory.

[39] - Cochran-Mantel-Haenszel test stratified by LDH level.

Secondary: Phase 1: Number of Participants With Adverse Events

| | |
|-----------------|---|
| End point title | Phase 1: Number of Participants With Adverse Events ^[40] |
|-----------------|---|

End point description:

The intensity of each adverse event (AE) was assessed utilizing the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 4.0, and according to the following: Grade 1 (Mild): AE is transient and easily tolerated by the participant; Grade 2 (Moderate): AE causes the participant discomfort and interrupts the participant's usual activities; Grade 3/4 (Severe): The adverse event causes considerable interference with the participant's usual activities and may be incapacitating or life-threatening; Grade 5: Death.

Serious adverse events were those that resulted in death, were life-threatening, required hospitalization or prolongation of hospitalization, resulted in congenital anomaly, or persistent or significant disability/incapacity.

The number of participants analyzed includes all participants enrolled in the Phase 1 portion of the study who received at least 1 dose of study treatment.

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

End point timeframe:

From first dose of any study drug to 30 days after the last dose; the median duration of treatment with veliparib across all groups in Phase 1 was 127.5 days.

Notes:

[40] - 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: Endpoint pertains to Phase 1 only.

| End point values | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Eto poside |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 3 | 4 | 3 |
| Units: participants | | | | |
| Any adverse event | 4 | 3 | 4 | 3 |

| | | | | |
|---------------------------|---|---|---|---|
| Any AE Grade 3/4 | 4 | 3 | 4 | 3 |
| Any serious adverse event | 3 | 1 | 3 | 2 |
| Any fatal adverse event | 0 | 0 | 1 | 1 |

| End point values | Phase 1: Veliparib 240 mg BID 7 Days + Carboplatin/Eto poside | Phase 1: Veliparib 240 mg BID 14 Days + Carboplatin/Eto poside | Phase 1: Veliparib 240 mg BID 21 Days + Carboplatin/Eto poside | |
|-----------------------------|--|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 8 | 14 | 4 | |
| Units: participants | | | | |
| Any adverse event | 8 | 14 | 4 | |
| Any AE Grade 3/4 | 7 | 14 | 4 | |
| Any serious adverse event | 3 | 6 | 3 | |
| Any fatal adverse event | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Deaths are reported from enrollment to end of study, maximum time on follow-up was 26 months. AEs were collected from first dose of study drug until 30 days after last dose; Maximum duration of treatment was 541 days in Phase 1 and 654 days in Phase 2.

Adverse event reporting additional description:

Adverse events and deaths are reported for all participants who received at least 1 dose of study drug (safety population). One participant randomized in Phase 2 to Arm A died before receiving treatment and was not included in the safety population.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Etoposide |
|-----------------------|---|

Reporting group description:

Participants received 80 mg veliparib orally twice a day (BID) on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered intravenously (IV) on Day 1 at a target area under the curve (AUC) 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|--|
| Reporting group title | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Etoposide |
|-----------------------|--|

Reporting group description:

Participants received 120 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|--|
| Reporting group title | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Etoposide |
|-----------------------|--|

Reporting group description:

Participants received 160 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|--|
| Reporting group title | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Etoposide |
|-----------------------|--|

Reporting group description:

Participants received 200 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle. Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|--|
| Reporting group title | Phase 1: Veliparib 240 mg BID 7 Days + Carboplatin/Etoposide |
|-----------------------|--|

Reporting group description:

Participants received 240 mg veliparib orally BID on Days -2 to 5 (7 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 5 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 1: Veliparib 240 mg BID 21 Days + Carboplatin/Etoposide |
|-----------------------|---|

Reporting group description:

Participants received 240 mg veliparib orally BID on Days -2 to Day 19 (continuous schedule) in combination with carboplatin/etoposide for up to four 21-day cycles. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 1: Veliparib 240 mg BID 14 Days + Carboplatin/Etoposide |
|-----------------------|---|

Reporting group description:

Participants received 240 mg veliparib orally BID on Days -2 to 12 (14 days) in combination with carboplatin/etoposide for up to four 21-day cycles, with the exception of Cycle 2, when veliparib was administered on Days 2 to 12 to allow for evaluation of potential impact of veliparib on etoposide pharmacokinetics. Carboplatin was administered IV on Day 1 at a target AUC 5 mg/mL*minute and etoposide 100 mg/m² IV on Days 1 to 3 of every 21-day cycle.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 2: Veliparib + Carboplatin/Etoposide -> Placebo |
|-----------------------|---|

Reporting group description:

Participants in Arm B received veliparib 240 mg BID on Day -2 to 12 (14-day schedule), carboplatin AUC 5 mg/mL*min administered on Day 1, and etoposide 100 mg/m² administered on Days 1 to 3 of each 21-day cycle for up to 6 cycles.

Participants without evidence of disease progression received placebo monotherapy BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 2: Veliparib + Carboplatin/Etoposide -> Veliparib |
|-----------------------|---|

Reporting group description:

Participants in Arm A received veliparib 240 mg BID on Day -2 to 12 (14-day schedule), carboplatin AUC 5 mg/mL*min administered on Day 1, and etoposide 100 mg/m² administered on Days 1 to 3 of each 21-day cycle for up to 6 cycles.

Participants without evidence of disease progression continued on veliparib monotherapy at 400 mg BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| | |
|-----------------------|---|
| Reporting group title | Phase 2: Placebo + Carboplatin/Etoposide -> Placebo |
|-----------------------|---|

Reporting group description:

Participants in Arm C received placebo BID on Day -2 to 12 (14-day schedule), carboplatin AUC 5 mg/mL*min on Day 1, and etoposide 100 mg/m² on Days 1 to 3 of each 21-day cycle for up to 6 cycles. Participants without evidence of disease progression received placebo monotherapy BID continuous dosing (21-day cycles) until disease progression or unacceptable toxicity.

| Serious adverse events | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Etoposide |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | 1 / 3 (33.33%) | 3 / 4 (75.00%) |
| number of deaths (all causes) | 0 | 0 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| CANCER PAIN | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| MALIGNANT NEOPLASM PROGRESSION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| METASTASES TO CENTRAL NERVOUS SYSTEM | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 | | | |
| AORTITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| PERIPHERAL ARTERY THROMBOSIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| PERIPHERAL EMBOLISM | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUPERIOR VENA CAVA SYNDROME | | | |

| | | | |
|--|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| VENA CAVA THROMBOSIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| CHEST PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| DEATH | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| DISEASE PROGRESSION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| FATIGUE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 PHYSICAL HEALTH DETERIORATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| MALAISE | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| SUDDEN CARDIAC DEATH | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| SUDDEN DEATH | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 | | | |
| ACUTE RESPIRATORY DISTRESS SYNDROME | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| ACUTE RESPIRATORY FAILURE | | | |

| | | | |
|---|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| ATELECTASIS | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| CHRONIC OBSTRUCTIVE PULMONARY DISEASE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| DYSпноEA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| EPISTAXIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| HAEMOPTYSIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (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 ASPIRATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| PNEUMONITIS | | | |

| | | | |
|---|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 FAILURE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 | | | |
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| Investigations | | | |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| TRANSAMINASES INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| VASCULAR PROCEDURE COMPLICATION | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 | | | |
| ACUTE MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 FAILURE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| CARDIO-RESPIRATORY ARREST | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SINUS NODE DYSFUNCTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| VENTRICULAR TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 | | | |

| | | | |
|---|---------------|---------------|---------------|
| CEREBRAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| ISCHAEMIC STROKE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| MIGRAINE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| MOTOR DYSFUNCTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| TOXIC NEUROPATHY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| PANCYTOPENIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| COLITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| DIARRHOEA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| DUODENAL ULCER PERFORATION | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| GASTRIC PERFORATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| GASTRITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 INFLAMMATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| HAEMATEMESIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| ILEUS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTESTINAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| MOUTH HAEMORRHAGE | | | |

| | | | |
|---|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| PALATAL OEDEMA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| VOMITING | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| Hepatobiliary disorders | | | |
| HEPATIC FAILURE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 | | | |
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| Endocrine disorders | | | |
| DIABETES INSIPIDUS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| BURSITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 | | | |
| ABDOMINAL SEPSIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| ANAL ABSCESS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |

| | | | |
|---|---------------|---------------|---------------|
| BRONCHITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| CELLULITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| ENCEPHALITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| IMPLANT SITE CELLULITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| ORCHITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| PLEURAL INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA INFLUENZAL | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 LEGIONELLA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| SEPTIC SHOCK | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| DEHYDRATION | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (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 | Phase 1: Veliparib 200 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 240 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 240 mg BID 21 Days + Carboplatin/Etoposide |
|--|---|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 3 / 8 (37.50%) | 3 / 4 (75.00%) |
| number of deaths (all causes) | 1 | 0 | 0 |
| number of deaths resulting from adverse events | 1 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| CANCER PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| MALIGNANT NEOPLASM PROGRESSION | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| METASTASES TO CENTRAL NERVOUS SYSTEM | | | |

| | | | |
|---|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 | | | |
| AORTITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 / 4 (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 |
| PERIPHERAL ARTERY THROMBOSIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| PERIPHERAL EMBOLISM | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| SUPERIOR VENA CAVA SYNDROME | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| VENA CAVA THROMBOSIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (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 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---------------|----------------|---------------|
| ASTHENIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| CHEST PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| DEATH | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| DISEASE PROGRESSION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FATIGUE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 PHYSICAL HEALTH DETERIORATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| MALAISE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (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 |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| OEDEMA PERIPHERAL | | | |

| | | | |
|--|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 / 4 (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 |
| SUDDEN CARDIAC DEATH | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| SUDDEN DEATH | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 | | | |
| ACUTE RESPIRATORY DISTRESS SYNDROME | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| ACUTE RESPIRATORY FAILURE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| ATELECTASIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| CHRONIC OBSTRUCTIVE | | | |

| | | | |
|---|---------------|---------------|---------------|
| PULMONARY DISEASE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| DYSпноEA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| EPISTAXIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| HAEMOPTYSIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 ASPIRATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| PNEUMONITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 / 4 (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 HAEMORRHAGE | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 FAILURE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 | | | |
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| Investigations | | | |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRANSAMINASES INCREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 | | | |
| VASCULAR PROCEDURE COMPLICATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 | | | |
| ACUTE MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| ATRIAL FIBRILLATION | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CARDIAC FAILURE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| CARDIO-RESPIRATORY ARREST | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| SINUS NODE DYSFUNCTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| VENTRICULAR TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 | | | |
| CEREBRAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| HEADACHE | | | |

| | | | |
|---|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| ISCHAEMIC STROKE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| MIGRAINE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| MOTOR DYSFUNCTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| TOXIC NEUROPATHY | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (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 / 4 (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 | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 / 4 (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 |
| PANCYTOPENIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| COLITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| DIARRHOEA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| DUODENAL ULCER PERFORATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| GASTRIC PERFORATION | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| GASTRITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 INFLAMMATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| HAEMATEMESIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| ILEUS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| INTESTINAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MOUTH HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| PALATAL OEDEMA | | | |

| | | | |
|--|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| VOMITING | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| Hepatobiliary disorders | | | |
| HEPATIC FAILURE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 | | | |
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| Endocrine disorders | | | |
| DIABETES INSIPIDUS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| BACK PAIN | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BURSITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 | | | |
| ABDOMINAL SEPSIS | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| ANAL ABSCESS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| BRONCHITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| CELLULITIS | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| ENCEPHALITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| IMPLANT SITE CELLULITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| INFECTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| ORCHITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| PLEURAL INFECTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 / 4 (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 INFLUENZAL | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 LEGIONELLA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SEPTIC SHOCK | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| DEHYDRATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| HYPOKALAEMIA | | | |

| | | | |
|---|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| HYPOMAGNEAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (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 | Phase 1: Veliparib 240 mg BID 14 Days + Carboplatin/Etoposide | Phase 2: Veliparib + Carboplatin/Etoposide -> Placebo | Phase 2: Veliparib + Carboplatin/Etoposide -> Veliparib |
|--|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 14 (42.86%) | 39 / 58 (67.24%) | 33 / 60 (55.00%) |
| number of deaths (all causes) | 0 | 45 | 49 |
| number of deaths resulting from adverse events | 0 | 10 | 7 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| CANCER PAIN | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| MALIGNANT NEOPLASM PROGRESSION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 5 / 58 (8.62%) | 5 / 60 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 6 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 3 |
| METASTASES TO CENTRAL NERVOUS SYSTEM | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 4 / 58 (6.90%) | 2 / 60 (3.33%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |

| | | | |
|---|----------------|----------------|----------------|
| AORTITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| HYPOTENSION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| PERIPHERAL ARTERY THROMBOSIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| PERIPHERAL EMBOLISM | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| SUPERIOR VENA CAVA SYNDROME | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| VENA CAVA THROMBOSIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |

| | | | |
|---|----------------|----------------|----------------|
| CHEST PAIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 2 / 60 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEATH | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| DISEASE PROGRESSION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FATIGUE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GENERAL PHYSICAL HEALTH DETERIORATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| MALAISE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 58 (3.45%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PAIN | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| PYREXIA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 58 (3.45%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SUDDEN CARDIAC DEATH | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| SUDDEN DEATH | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| ACUTE RESPIRATORY DISTRESS SYNDROME | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| ACUTE RESPIRATORY FAILURE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| ATELECTASIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| CHRONIC OBSTRUCTIVE PULMONARY DISEASE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| DYSпноEA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 2 / 60 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EPISTAXIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMOPTYSIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 58 (5.17%) | 2 / 60 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA ASPIRATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 58 (3.45%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| PULMONARY HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| RESPIRATORY FAILURE | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Psychiatric disorders | | | |
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| Investigations | | | |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| TRANSAMINASES INCREASED | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 | | | |
| VASCULAR PROCEDURE COMPLICATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| Cardiac disorders | | | |
| ACUTE MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 2 / 60 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CARDIAC FAILURE | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CARDIO-RESPIRATORY ARREST | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| SINUS NODE DYSFUNCTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VENTRICULAR TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| CEREBRAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| ISCHAEMIC STROKE | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MIGRAINE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| MOTOR DYSFUNCTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| TOXIC NEUROPATHY | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 58 (5.17%) | 3 / 60 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEBRILE NEUTROPENIA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 7 / 58 (12.07%) | 5 / 60 (8.33%) |
| occurrences causally related to treatment / all | 1 / 1 | 5 / 7 | 2 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUTROPENIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 4 / 58 (6.90%) | 2 / 60 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 5 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PANCYTOPENIA | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 2 / 60 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 6 / 58 (10.34%) | 3 / 60 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 9 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| COLITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| DIARRHOEA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| DUODENAL ULCER PERFORATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| GASTRIC PERFORATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| GASTRITIS | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 INFLAMMATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| HAEMATEMESIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| ILEUS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| INTESTINAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| MOUTH HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 58 (3.45%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PALATAL OEDEMA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| VOMITING | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| HEPATIC FAILURE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| Endocrine disorders | | | |
| DIABETES INSIPIDUS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| BURSITIS | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| FLANK PAIN | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (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 PAIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 | | | |
| ABDOMINAL SEPSIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| ANAL ABSCESS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| BRONCHITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| CELLULITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| DEVICE RELATED INFECTION | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| ENCEPHALITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| IMPLANT SITE CELLULITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| INFECTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 58 (3.45%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ORCHITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PLEURAL INFECTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 58 (5.17%) | 7 / 60 (11.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 2 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| PNEUMONIA INFLUENZAL | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA LEGIONELLA | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| SEPTIC SHOCK | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (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 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 58 (3.45%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEHYDRATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 3 / 60 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (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 |
| HYPOMAGNESAEMIA | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 3 / 58 (5.17%) | 0 / 60 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|--|--|
| Serious adverse events | Phase 2: Placebo + Carboplatin/Etoposide -> Placebo | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 27 / 60 (45.00%) | | |
| number of deaths (all causes) | 41 | | |
| number of deaths resulting from adverse events | 5 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| CANCER PAIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| MALIGNANT NEOPLASM PROGRESSION | | | |
| subjects affected / exposed | 5 / 60 (8.33%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| METASTASES TO CENTRAL NERVOUS SYSTEM | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| AORTITIS | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HAEMORRHAGE | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HYPOTENSION | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PERIPHERAL ARTERY THROMBOSIS | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PERIPHERAL EMBOLISM | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SUPERIOR VENA CAVA SYNDROME | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| VENA CAVA THROMBOSIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CHEST PAIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DEATH | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| DISEASE PROGRESSION | | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| FATIGUE | | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| GENERAL PHYSICAL HEALTH DETERIORATION | | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| MALAISE | | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| NON-CARDIAC CHEST PAIN | | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| OEDEMA PERIPHERAL | | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PAIN | | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PYREXIA | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SUDDEN CARDIAC DEATH | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| SUDDEN DEATH | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| ACUTE RESPIRATORY DISTRESS SYNDROME | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| ACUTE RESPIRATORY FAILURE | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ATELECTASIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CHRONIC OBSTRUCTIVE PULMONARY DISEASE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DYSпноEA | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| EPISTAXIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HAEMOPTYSIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PNEUMONIA ASPIRATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PNEUMONITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PULMONARY HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| RESPIRATORY FAILURE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |

| | | | |
|---|----------------|--|--|
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| TRANSAMINASES INCREASED | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| VASCULAR PROCEDURE COMPLICATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| ACUTE MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CARDIAC FAILURE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CARDIO-RESPIRATORY ARREST | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SINUS NODE DYSFUNCTION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| VENTRICULAR TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| CEREBRAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ISCHAEMIC STROKE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| MIGRAINE | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| MOTOR DYSFUNCTION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| TOXIC NEUROPATHY | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| FEBRILE NEUTROPENIA | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LEUKOPENIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| NEUTROPENIA | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PANCYTOPENIA | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| THROMBOCYTOPENIA | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COLITIS | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DIARRHOEA | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DUODENAL ULCER PERFORATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DYSPHAGIA | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| GASTRIC PERFORATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| GASTRITIS | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| GASTROINTESTINAL INFLAMMATION | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HAEMATEMESIS | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| ILEUS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| INTESTINAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| MOUTH HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| NAUSEA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PALATAL OEDEMA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| VOMITING | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| HEPATIC FAILURE | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| DIABETES INSIPIDUS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| BACK PAIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| BURSITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| FLANK PAIN | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| ABDOMINAL SEPSIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ANAL ABSCESS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| BRONCHITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CELLULITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ENCEPHALITIS | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| IMPLANT SITE CELLULITIS | | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| INFECTION | | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| ORCHITIS | | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PLEURAL INFECTION | | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PNEUMONIA | | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PNEUMONIA INFLUENZAL | | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PNEUMONIA LEGIONELLA | | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| RESPIRATORY TRACT INFECTION | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SEPSIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SEPTIC SHOCK | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DEHYDRATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HYPONATRAEMIA | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Phase 1: Veliparib 80 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 120 mg BID 7 Days + Carboplatin/Etoposide | Phase 1: Veliparib 160 mg BID 7 Days + Carboplatin/Etoposide |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | 3 / 3 (100.00%) | 4 / 4 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| CANCER PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MALIGNANT NEOPLASM PROGRESSION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| METASTASES TO CENTRAL NERVOUS SYSTEM | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vascular disorders | | | |
| HAEMATOMA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HOT FLUSH | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| HYPERTENSION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| HYPOTENSION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| INTERMITTENT CLAUDICATION | | | |

| | | | |
|--|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| CHEST PAIN | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| CREPITATIONS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CRYING | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FACE OEDEMA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FATIGUE | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 3 / 3 (100.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 3 | 5 | 2 |
| FEELING ABNORMAL | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FEELING COLD | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| GAIT DISTURBANCE | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 4 |
| INJECTION SITE EXTRAVASATION | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INJECTION SITE HAEMATOMA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| INJECTION SITE PHLEBITIS | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| LOSS OF CONTROL OF LEGS | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| MALAISE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NECROSIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OEDEMA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 0 | 1 |
| PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| SWELLING | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| SWELLING FACE subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Immune system disorders DRUG HYPERSENSITIVITY subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Reproductive system and breast disorders PERINEAL PAIN subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders ASTHMA subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| COUGH subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 2 / 4 (50.00%) 2 |
| DYSPHONIA subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| DYSPNOEA subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 4 | 1 / 3 (33.33%) 1 | 1 / 4 (25.00%) 2 |
| EPISTAXIS subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| HAEMOPTYSIS subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| HICCUPS subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 4 (0.00%) 0 |
| OROPHARYNGEAL PAIN | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| PRODUCTIVE COUGH | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RHINITIS ALLERGIC | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RHINORRHOEA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONFUSIONAL STATE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DELIRIUM | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| HALLUCINATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INSOMNIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| RESTLESSNESS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|----------------|---------------|----------------|
| TENSION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Product issues | | | |
| DEVICE OCCLUSION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD CREATININE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| BLOOD LACTATE DEHYDROGENASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GAMMA-GLUTAMYLTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HLA MARKER STUDY POSITIVE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INTERNATIONAL NORMALISED RATIO INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| LYMPHOCYTE COUNT DECREASED | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NEUTROPHIL COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 5 | 1 |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| TRANSAMINASES INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINE OUTPUT DECREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| WEIGHT INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 2 / 4 (50.00%) |
| occurrences (all) | 0 | 1 | 3 |
| WHITE BLOOD CELL COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| CHEMICAL PHLEBITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| FOREARM FRACTURE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INFUSION RELATED REACTION | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| MUSCLE RUPTURE | | | |

| | | | |
|------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| MUSCLE STRAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POST PROCEDURAL COMPLICATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROCEDURAL HEADACHE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SKIN ABRASION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LEFT VENTRICULAR FAILURE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PALPITATIONS | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| ATAXIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| DISTURBANCE IN ATTENTION | | | |

| | | | |
|------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DIZZINESS | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| DYSARTHRIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSGEUSIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| HEAD DISCOMFORT | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| MEMORY IMPAIRMENT | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE CONTRACTIONS INVOLUNTARY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NEUROPATHY PERIPHERAL | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| PERIPHERAL MOTOR NEUROPATHY | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 2 | 0 | 1 |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 2 / 3 (66.67%) | 1 / 4 (25.00%) |
| occurrences (all) | 2 | 2 | 1 |
| POLYNEUROPATHY | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--|----------------|----------------|----------------|
| PRESYNCOPE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| SOMNOLENCE | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| TREMOR | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 3 (33.33%) | 2 / 4 (50.00%) |
| occurrences (all) | 3 | 1 | 9 |
| DISSEMINATED INTRAVASCULAR COAGULATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FEBRILE NEUTROPENIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| NEUTROPENIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 4 | 0 | 8 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Ear and labyrinth disorders | | | |
| EAR DISCOMFORT | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 2 |
| HYPOACUSIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OTOTOXICITY | | | |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| TINNITUS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| BLINDNESS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DRY EYE | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| EYE IRRITATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EYE PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LACRIMATION INCREASED | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VITREOUS DETACHMENT | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISCOMFORT | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 0 | 0 | 3 |
| ABDOMINAL PAIN UPPER | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| ANAL INFLAMMATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ASCITES | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| CONSTIPATION | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences (all) | 2 | 1 | 1 |
| DIARRHOEA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 3 (33.33%) | 2 / 4 (50.00%) |
| occurrences (all) | 1 | 1 | 4 |
| DIVERTICULUM | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| DRY MOUTH | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| DYSPEPSIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ENTEROVESICAL FISTULA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| ERUCTATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FLATULENCE | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 0 | 1 |
| GASTRITIS | | | |

| | | | |
|------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMATOCHEZIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMORRHOIDS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LOWER GASTROINTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAUSEA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 3 (66.67%) | 2 / 4 (50.00%) |
| occurrences (all) | 1 | 4 | 7 |
| OESOPHAGITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ORAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROCTALGIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROCTITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RETCHING | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| STOMATITIS | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VOMITING | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 2 / 3 (66.67%) | 3 / 4 (75.00%) |
| occurrences (all) | 2 | 2 | 4 |
| Hepatobiliary disorders | | | |
| HEPATIC PAIN | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| ALOPECIA | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 1 / 3 (33.33%) | 2 / 4 (50.00%) |
| occurrences (all) | 2 | 1 | 3 |
| DRY SKIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| ECCHYMOSIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ECZEMA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERHIDROSIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| NIGHT SWEATS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PETECHIAE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| PIGMENTATION DISORDER | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PRURITUS | | | |

| | | | |
|------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 0 | 1 |
| RASH | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RASH MACULAR | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SKIN ULCER | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| STICKY SKIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| DYSURIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| NOCTURIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PNEUMATURIA | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| POST MICTURITION DRIBBLE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TUBULOINTERSTITIAL NEPHRITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY HESITATION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY INCONTINENCE | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| URINARY RETENTION subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Endocrine disorders INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 4 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| BACK PAIN subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 2 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| BONE PAIN subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| COCCYDYNIA subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| FLANK PAIN subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 4 (0.00%) 0 |
| GROIN PAIN subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| INTERVERTEBRAL DISC PROTRUSION subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| MUSCLE SPASMS subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 3 (33.33%) 2 | 2 / 4 (50.00%) 2 |
| MUSCULAR WEAKNESS subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |

| | | | |
|-------------------------------|----------------|----------------|----------------|
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULOSKELETAL STIFFNESS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MYALGIA | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | 1 / 3 (33.33%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| MYOSITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NECK PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 3 (66.67%) | 2 / 4 (50.00%) |
| occurrences (all) | 1 | 2 | 2 |
| PAIN IN JAW | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SPINAL PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TENDON PAIN | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| BRONCHITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CLOSTRIDIUM DIFFICILE COLITIS | | | |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CYSTITIS | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 3 (33.33%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| ORAL CANDIDIASIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ORAL FUNGAL INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RHINITIS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 2 |
| TOOTH ABSCESS | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 3 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---------------------|---------------------|---------------------|
| URINARY TRACT INFECTION subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 2 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 2 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 3 | 2 / 3 (66.67%) 4 | 3 / 4 (75.00%) 3 |
| DEHYDRATION subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| HYPERGLYCAEMIA subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| HYPERKALAEMIA subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| HYPOCALCAEMIA subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| HYPOGLYCAEMIA subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| HYPOKALAEMIA subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 3 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| HYPOMAGNESAEMIA subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 1 / 3 (33.33%) 1 | 0 / 4 (0.00%) 0 |
| HYPONATRAEMIA subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| HYPOPHOSPHATAEMIA subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 4 (0.00%) 0 |

| | | | |
|-----------------------------------|--|--|---|
| Non-serious adverse events | Phase 1: Veliparib 200 mg BID 7 Days + | Phase 1: Veliparib 240 mg BID 7 Days + | Phase 1: Veliparib 240 mg BID 21 Days + |
|-----------------------------------|--|--|---|

| | Carboplatin/Etoposide | Carboplatin/Etoposide | Carboplatin/Etoposide |
|---|-----------------------|-----------------------|-----------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 8 / 8 (100.00%) | 4 / 4 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| CANCER PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| MALIGNANT NEOPLASM PROGRESSION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| METASTASES TO CENTRAL NERVOUS SYSTEM | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| HAEMATOMA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| HOT FLUSH | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERTENSION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOTENSION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INTERMITTENT CLAUDICATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (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 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| CHEST PAIN | | | |

| | | | |
|------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| CREPITATIONS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CRYING | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FACE OEDEMA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| FATIGUE | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 6 / 8 (75.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 4 | 6 | 1 |
| FEELING ABNORMAL | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| FEELING COLD | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GAIT DISTURBANCE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| INJECTION SITE EXTRAVASATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INJECTION SITE HAEMATOMA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INJECTION SITE PHLEBITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LOSS OF CONTROL OF LEGS | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MALAISE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NECROSIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| OEDEMA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PYREXIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| SWELLING | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SWELLING FACE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| DRUG HYPERSENSITIVITY | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|----------------|----------------|----------------|
| Reproductive system and breast disorders | | | |
| PERINEAL PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| ASTHMA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| COUGH | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 1 | 0 | 2 |
| DYSPHONIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| DYSPNOEA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 8 (12.50%) | 2 / 4 (50.00%) |
| occurrences (all) | 1 | 1 | 2 |
| EPISTAXIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 3 |
| HAEMOPTYSIS | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| HICCUPS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PRODUCTIVE COUGH | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RHINITIS ALLERGIC | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| RHINORRHOEA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 8 (25.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| CONFUSIONAL STATE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DELIRIUM | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 2 |
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| HALLUCINATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| INSOMNIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 8 (37.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 3 | 1 |
| RESTLESSNESS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| TENSION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Product issues | | | |
| DEVICE OCCLUSION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Investigations | | | |

| | | | |
|--|----------------|----------------|----------------|
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 2 |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 2 |
| BLOOD CREATININE INCREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| BLOOD LACTATE DEHYDROGENASE INCREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GAMMA-GLUTAMYLTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HLA MARKER STUDY POSITIVE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| INTERNATIONAL NORMALISED RATIO INCREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LYMPHOCYTE COUNT DECREASED | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| NEUTROPHIL COUNT DECREASED | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 8 (12.50%) | 2 / 4 (50.00%) |
| occurrences (all) | 2 | 2 | 8 |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 3 |
| TRANSAMINASES INCREASED | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINE OUTPUT DECREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| WEIGHT INCREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| WHITE BLOOD CELL COUNT DECREASED | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 1 | 0 | 3 |
| Injury, poisoning and procedural complications | | | |
| CHEMICAL PHLEBITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FOREARM FRACTURE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| INFUSION RELATED REACTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE RUPTURE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE STRAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POST PROCEDURAL COMPLICATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| PROCEDURAL HEADACHE | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 4 (0.00%) 0 |
| PROCEDURAL PAIN subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| SKIN ABRASION subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Cardiac disorders ATRIAL FIBRILLATION subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 8 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| LEFT VENTRICULAR FAILURE subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| PALPITATIONS subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| TACHYCARDIA subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Nervous system disorders ATAXIA subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| DISTURBANCE IN ATTENTION subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 8 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| DIZZINESS subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 8 (12.50%) 4 | 2 / 4 (50.00%) 2 |
| DYSARTHRIA subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 4 (0.00%) 0 |
| DYSGEUSIA | | | |

| | | | |
|---------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 2 / 4 (50.00%) |
| occurrences (all) | 0 | 1 | 2 |
| HEAD DISCOMFORT | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| HEADACHE | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 8 (25.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| MEMORY IMPAIRMENT | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| MUSCLE CONTRACTIONS INVOLUNTARY | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NEUROPATHY PERIPHERAL | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PERIPHERAL MOTOR NEUROPATHY | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| POLYNEUROPATHY | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PRESYNCOPE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SOMNOLENCE | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 0 | 2 |
| TREMOR | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|----------------|----------------|----------------|
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 4 / 8 (50.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 3 | 11 | 6 |
| DISSEMINATED INTRAVASCULAR COAGULATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| FEBRILE NEUTROPENIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 8 (25.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| NEUTROPENIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 8 (50.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 0 | 11 | 6 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 8 (37.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 6 | 3 |
| Ear and labyrinth disorders | | | |
| EAR DISCOMFORT | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOACUSIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| OTOTOXICITY | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TINNITUS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |
| BLINDNESS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|-----------------------------|---------------|----------------|----------------|
| DRY EYE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EYE IRRITATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| EYE PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LACRIMATION INCREASED | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| VITREOUS DETACHMENT | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 8 (37.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 3 | 3 |
| ANAL INFLAMMATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ASCITES | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONSTIPATION | | | |

| | | | |
|----------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 8 (37.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| DIARRHOEA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| DIVERTICULUM | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DRY MOUTH | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 8 (25.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 2 | 1 |
| DYSPEPSIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 8 (25.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ENTEROVESICAL FISTULA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ERUCTATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FLATULENCE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTRITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMATOCHEZIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--|----------------|----------------|----------------|
| HAEMORRHOIDS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| LOWER GASTROINTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NAUSEA | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 5 / 8 (62.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 4 | 8 | 1 |
| OESOPHAGITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ORAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PROCTALGIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROCTITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RETCHING | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| STOMATITIS | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| VOMITING | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 8 (12.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 2 | 2 | 1 |
| Hepatobiliary disorders | | | |
| HEPATIC PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| ALOPECIA | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 3 / 8 (37.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 2 | 5 | 3 |
| DRY SKIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| ECCHYMOSIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| ECZEMA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERHIDROSIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| NIGHT SWEATS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PETECHIAE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PIGMENTATION DISORDER | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PRURITUS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RASH | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RASH MACULAR | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| SKIN ULCER | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---------------------|---------------------|---------------------|
| STICKY SKIN subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Renal and urinary disorders | | | |
| DYSURIA subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| NOCTURIA subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| PNEUMATURIA subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| POST MICTURITION DRIBBLE subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 4 (0.00%) 0 |
| TUBULOINTERSTITIAL NEPHRITIS subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 8 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| URINARY HESITATION subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 4 (0.00%) 0 |
| URINARY INCONTINENCE subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 8 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| URINARY RETENTION subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 8 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Endocrine disorders | | | |
| INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 8 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 2 / 8 (25.00%) 3 | 0 / 4 (0.00%) 0 |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| BACK PAIN | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 2 / 8 (25.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| BONE PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 8 (25.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 2 | 1 |
| COCCYDYNIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| GROIN PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INTERVERTEBRAL DISC PROTRUSION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| MUSCULOSKELETAL STIFFNESS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MYALGIA | | | |

| | | | |
|-------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| MYOSITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NECK PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| PAIN IN JAW | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SPINAL PAIN | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| TENDON PAIN | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| BRONCHITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CLOSTRIDIUM DIFFICILE COLITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|------------------------------------|----------------|----------------|----------------|
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ORAL CANDIDIASIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ORAL FUNGAL INFECTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| PNEUMONIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| RHINITIS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TOOTH ABSCESS | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 8 (37.50%) | 2 / 4 (50.00%) |
| occurrences (all) | 0 | 5 | 2 |
| DEHYDRATION | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPERGLYCAEMIA | | | |

| | | | |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 8 (25.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| HYPERKALAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| HYPOCALCAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOGLYCAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 8 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 3 |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 8 (25.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 3 | 1 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| HYPOPHOSPHATAEMIA | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 8 (12.50%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| Non-serious adverse events | Phase 1: Veliparib 240 mg BID 14 Days + Carboplatin/Etoposide | Phase 2: Veliparib + Carboplatin/Etoposide -> Placebo | Phase 2: Veliparib + Carboplatin/Etoposide -> Veliparib |
|---|--|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 14 / 14 (100.00%) | 53 / 58 (91.38%) | 57 / 60 (95.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| CANCER PAIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| MALIGNANT NEOPLASM PROGRESSION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--|-----------------|------------------|-----------------|
| METASTASES TO CENTRAL NERVOUS SYSTEM | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Vascular disorders | | | |
| HAEMATOMA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| HOT FLUSH | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 58 (5.17%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| HYPERTENSION | | | |
| subjects affected / exposed | 4 / 14 (28.57%) | 1 / 58 (1.72%) | 2 / 60 (3.33%) |
| occurrences (all) | 6 | 3 | 2 |
| HYPOTENSION | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 5 / 58 (8.62%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 5 | 1 |
| INTERMITTENT CLAUDICATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 11 / 58 (18.97%) | 9 / 60 (15.00%) |
| occurrences (all) | 8 | 26 | 16 |
| CHEST PAIN | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 3 / 58 (5.17%) | 3 / 60 (5.00%) |
| occurrences (all) | 2 | 3 | 3 |
| CREPITATIONS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| CRYING | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| FACE OEDEMA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FATIGUE | | | |

| | | | |
|------------------------------|-----------------|------------------|------------------|
| subjects affected / exposed | 9 / 14 (64.29%) | 16 / 58 (27.59%) | 15 / 60 (25.00%) |
| occurrences (all) | 20 | 17 | 23 |
| FEELING ABNORMAL | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FEELING COLD | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 58 (3.45%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| GAIT DISTURBANCE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| INJECTION SITE EXTRAVASATION | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| INJECTION SITE HAEMATOMA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INJECTION SITE PHLEBITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LOSS OF CONTROL OF LEGS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MALAISE | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 3 / 58 (5.17%) | 0 / 60 (0.00%) |
| occurrences (all) | 3 | 3 | 0 |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 58 (3.45%) | 2 / 60 (3.33%) |
| occurrences (all) | 1 | 2 | 2 |
| NECROSIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NON-CARDIAC CHEST PAIN | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 58 (3.45%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 2 | 1 |
| OEDEMA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 6 / 58 (10.34%) | 2 / 60 (3.33%) |
| occurrences (all) | 3 | 7 | 3 |
| PAIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 58 (5.17%) | 4 / 60 (6.67%) |
| occurrences (all) | 0 | 3 | 4 |
| PYREXIA | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 2 / 58 (3.45%) | 6 / 60 (10.00%) |
| occurrences (all) | 3 | 2 | 9 |
| SWELLING | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SWELLING FACE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 58 (3.45%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Immune system disorders | | | |
| DRUG HYPERSENSITIVITY | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Reproductive system and breast disorders | | | |
| PERINEAL PAIN | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| ASTHMA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| COUGH | | | |
| subjects affected / exposed | 5 / 14 (35.71%) | 5 / 58 (8.62%) | 6 / 60 (10.00%) |
| occurrences (all) | 6 | 5 | 6 |
| DYSPHONIA | | | |

| | | | |
|-----------------------------|-----------------|-----------------|------------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 3 / 58 (5.17%) | 2 / 60 (3.33%) |
| occurrences (all) | 1 | 4 | 2 |
| DYSпноEA | | | |
| subjects affected / exposed | 5 / 14 (35.71%) | 9 / 58 (15.52%) | 12 / 60 (20.00%) |
| occurrences (all) | 5 | 11 | 16 |
| EPISTAXIS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| HAEMOPTYSIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 58 (3.45%) | 2 / 60 (3.33%) |
| occurrences (all) | 0 | 2 | 2 |
| HICCUPS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 3 / 58 (5.17%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 3 | 1 |
| PRODUCTIVE COUGH | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 4 / 58 (6.90%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 6 | 1 |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 58 (3.45%) | 3 / 60 (5.00%) |
| occurrences (all) | 0 | 2 | 3 |
| RHINITIS ALLERGIC | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| RHINORRHOEA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 58 (5.17%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 3 | 1 |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 4 / 58 (6.90%) | 3 / 60 (5.00%) |
| occurrences (all) | 0 | 4 | 3 |
| CONFUSIONAL STATE | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |

| | | | |
|--------------------------------------|-----------------|----------------|----------------|
| DELIRIUM | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| HALLUCINATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INSOMNIA | | | |
| subjects affected / exposed | 7 / 14 (50.00%) | 5 / 58 (8.62%) | 4 / 60 (6.67%) |
| occurrences (all) | 11 | 6 | 5 |
| RESTLESSNESS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TENSION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Product issues | | | |
| DEVICE OCCLUSION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 3 / 58 (5.17%) | 5 / 60 (8.33%) |
| occurrences (all) | 1 | 6 | 5 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 3 / 58 (5.17%) | 5 / 60 (8.33%) |
| occurrences (all) | 1 | 4 | 6 |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 2 / 60 (3.33%) |
| occurrences (all) | 0 | 0 | 2 |
| BLOOD CREATININE INCREASED | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 4 / 60 (6.67%) |
| occurrences (all) | 0 | 1 | 4 |
| BLOOD LACTATE DEHYDROGENASE | | | |

| | | | |
|---|-----------------|----------------|----------------|
| INCREASED | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 3 / 60 (5.00%) |
| occurrences (all) | 0 | 1 | 3 |
| GAMMA-GLUTAMYLTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| HLA MARKER STUDY POSITIVE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INTERNATIONAL NORMALISED RATIO INCREASED | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| LYMPHOCYTE COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NEUTROPHIL COUNT DECREASED | | | |
| subjects affected / exposed | 6 / 14 (42.86%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 20 | 0 | 2 |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 5 / 14 (35.71%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences (all) | 11 | 6 | 2 |
| TRANSAMINASES INCREASED | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| URINE OUTPUT DECREASED | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 5 / 14 (35.71%) | 2 / 58 (3.45%) | 3 / 60 (5.00%) |
| occurrences (all) | 13 | 2 | 3 |
| WEIGHT INCREASED | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 2 / 60 (3.33%) |
| occurrences (all) | 0 | 0 | 3 |
| WHITE BLOOD CELL COUNT DECREASED | | | |

| | | | |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 2 / 14 (14.29%) 2 | 1 / 58 (1.72%) 2 | 1 / 60 (1.67%) 5 |
| Injury, poisoning and procedural complications | | | |
| CHEMICAL PHLEBITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FOREARM FRACTURE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| INFUSION RELATED REACTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| MUSCLE RUPTURE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE STRAIN | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| POST PROCEDURAL COMPLICATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROCEDURAL HEADACHE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SKIN ABRASION | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac disorders | | | |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 5 / 58 (8.62%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 5 | 1 |
| LEFT VENTRICULAR FAILURE | | | |

| | | | |
|------------------------------------|-----------------|-----------------|------------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PALPITATIONS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 3 / 60 (5.00%) |
| occurrences (all) | 0 | 0 | 4 |
| TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Nervous system disorders | | | |
| ATAXIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DISTURBANCE IN ATTENTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DIZZINESS | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 9 / 58 (15.52%) | 5 / 60 (8.33%) |
| occurrences (all) | 6 | 13 | 6 |
| DYSARTHRIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DYSGEUSIA | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 4 / 58 (6.90%) | 2 / 60 (3.33%) |
| occurrences (all) | 3 | 6 | 2 |
| HEAD DISCOMFORT | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| HEADACHE | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 9 / 58 (15.52%) | 10 / 60 (16.67%) |
| occurrences (all) | 3 | 11 | 11 |
| MEMORY IMPAIRMENT | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| MUSCLE CONTRACTIONS INVOLUNTARY | | | |

| | | | |
|--|-----------------|------------------|------------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| NEUROPATHY PERIPHERAL | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PERIPHERAL MOTOR NEUROPATHY | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 0 | 1 |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 3 / 60 (5.00%) |
| occurrences (all) | 0 | 1 | 3 |
| POLYNEUROPATHY | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PRESYNCOPE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SOMNOLENCE | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| TREMOR | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 7 / 14 (50.00%) | 35 / 58 (60.34%) | 35 / 60 (58.33%) |
| occurrences (all) | 18 | 105 | 104 |
| DISSEMINATED INTRAVASCULAR COAGULATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FEBRILE NEUTROPENIA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 0 | 1 |
| LEUKOPENIA | | | |

| | | | |
|-----------------------------|-----------------|------------------|------------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 12 / 58 (20.69%) | 7 / 60 (11.67%) |
| occurrences (all) | 0 | 27 | 15 |
| NEUTROPENIA | | | |
| subjects affected / exposed | 8 / 14 (57.14%) | 33 / 58 (56.90%) | 36 / 60 (60.00%) |
| occurrences (all) | 34 | 86 | 94 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 5 / 14 (35.71%) | 23 / 58 (39.66%) | 22 / 60 (36.67%) |
| occurrences (all) | 16 | 62 | 58 |
| Ear and labyrinth disorders | | | |
| EAR DISCOMFORT | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HYPOACUSIS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| OTOTOXICITY | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TINNITUS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Eye disorders | | | |
| BLINDNESS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DRY EYE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EYE IRRITATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| EYE PAIN | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| LACRIMATION INCREASED | | | |

| | | | |
|-----------------------------|-----------------|------------------|------------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| VITREOUS DETACHMENT | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISCOMFORT | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 2 / 60 (3.33%) |
| occurrences (all) | 2 | 1 | 2 |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 1 / 58 (1.72%) | 4 / 60 (6.67%) |
| occurrences (all) | 2 | 1 | 4 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 58 (0.00%) | 2 / 60 (3.33%) |
| occurrences (all) | 2 | 0 | 2 |
| ANAL INFLAMMATION | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| ASCITES | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CONSTIPATION | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 13 / 58 (22.41%) | 14 / 60 (23.33%) |
| occurrences (all) | 4 | 19 | 17 |
| DIARRHOEA | | | |
| subjects affected / exposed | 7 / 14 (50.00%) | 11 / 58 (18.97%) | 8 / 60 (13.33%) |
| occurrences (all) | 11 | 21 | 11 |
| DIVERTICULUM | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| DRY MOUTH | | | |
| subjects affected / exposed | 4 / 14 (28.57%) | 3 / 58 (5.17%) | 1 / 60 (1.67%) |
| occurrences (all) | 5 | 4 | 1 |

| | | | |
|------------------------------------|-----------------|------------------|------------------|
| DYSPEPSIA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 58 (3.45%) | 7 / 60 (11.67%) |
| occurrences (all) | 1 | 3 | 8 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 2 / 60 (3.33%) |
| occurrences (all) | 1 | 1 | 2 |
| ENTEROVESICAL FISTULA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ERUCTATION | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| FLATULENCE | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 2 / 58 (3.45%) | 0 / 60 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| GASTRITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 58 (3.45%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 2 | 2 |
| HAEMATOCHEZIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| HAEMORRHOIDS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| LOWER GASTROINTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| NAUSEA | | | |
| subjects affected / exposed | 9 / 14 (64.29%) | 23 / 58 (39.66%) | 29 / 60 (48.33%) |
| occurrences (all) | 16 | 47 | 57 |
| OESOPHAGITIS | | | |

| | | | |
|--|-----------------|------------------|------------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 1 | 2 |
| ORAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PROCTALGIA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| PROCTITIS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| RETCHING | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| STOMATITIS | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 2 / 58 (3.45%) | 3 / 60 (5.00%) |
| occurrences (all) | 3 | 2 | 4 |
| VOMITING | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 10 / 58 (17.24%) | 13 / 60 (21.67%) |
| occurrences (all) | 3 | 12 | 20 |
| Hepatobiliary disorders | | | |
| HEPATIC PAIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| ALOPECIA | | | |
| subjects affected / exposed | 8 / 14 (57.14%) | 17 / 58 (29.31%) | 22 / 60 (36.67%) |
| occurrences (all) | 12 | 19 | 27 |
| DRY SKIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| ECCHYMOSIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| ECZEMA | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| HYPERHIDROSIS | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 4 | 0 | 1 |
| NIGHT SWEATS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| PETECHIAE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PIGMENTATION DISORDER | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| PRURITUS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 2 | 1 |
| RASH | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 4 / 60 (6.67%) |
| occurrences (all) | 1 | 1 | 4 |
| RASH MACULAR | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| SKIN ULCER | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| STICKY SKIN | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| DYSURIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| NOCTURIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| PNEUMATURIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| POST MICTURITION DRIBBLE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| TUBULOINTERSTITIAL NEPHRITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY HESITATION | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| URINARY INCONTINENCE | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| URINARY RETENTION | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 1 | 2 |
| Endocrine disorders | | | |
| INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 58 (3.45%) | 6 / 60 (10.00%) |
| occurrences (all) | 4 | 6 | 8 |
| BACK PAIN | | | |
| subjects affected / exposed | 6 / 14 (42.86%) | 7 / 58 (12.07%) | 9 / 60 (15.00%) |
| occurrences (all) | 6 | 7 | 11 |
| BONE PAIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 3 / 60 (5.00%) |
| occurrences (all) | 0 | 1 | 3 |
| COCCYDYNIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| FLANK PAIN | | | |

| | | | |
|--------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 0 | 1 |
| GROIN PAIN | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| INTERVERTEBRAL DISC PROTRUSION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 2 / 60 (3.33%) |
| occurrences (all) | 0 | 0 | 2 |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 58 (3.45%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 3 / 58 (5.17%) | 5 / 60 (8.33%) |
| occurrences (all) | 1 | 7 | 5 |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 2 / 58 (3.45%) | 3 / 60 (5.00%) |
| occurrences (all) | 3 | 2 | 3 |
| MUSCULOSKELETAL STIFFNESS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| MYALGIA | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 2 / 58 (3.45%) | 1 / 60 (1.67%) |
| occurrences (all) | 2 | 8 | 1 |
| MYOSITIS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| NECK PAIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 3 / 60 (5.00%) |
| occurrences (all) | 0 | 1 | 4 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 4 / 14 (28.57%) | 4 / 58 (6.90%) | 1 / 60 (1.67%) |
| occurrences (all) | 6 | 4 | 2 |

| | | | |
|-------------------------------|----------------|----------------|----------------|
| PAIN IN JAW | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 0 | 1 |
| SPINAL PAIN | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| TENDON PAIN | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |
| BRONCHITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 58 (5.17%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 3 | 1 |
| CLOSTRIDIUM DIFFICILE COLITIS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 58 (3.45%) | 2 / 60 (3.33%) |
| occurrences (all) | 1 | 3 | 2 |
| ORAL CANDIDIASIS | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 4 / 58 (6.90%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 4 | 2 |
| ORAL FUNGAL INFECTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| PNEUMONIA | | | |

| | | | |
|------------------------------------|-----------------|------------------|------------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 5 / 60 (8.33%) |
| occurrences (all) | 0 | 0 | 5 |
| RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 58 (5.17%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 3 | 1 |
| RHINITIS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 1 | 1 |
| TOOTH ABSCESS | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 58 (0.00%) | 0 / 60 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 2 / 58 (3.45%) | 0 / 60 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 58 (3.45%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 3 | 1 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 7 / 14 (50.00%) | 12 / 58 (20.69%) | 17 / 60 (28.33%) |
| occurrences (all) | 16 | 14 | 20 |
| DEHYDRATION | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 58 (5.17%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 3 | 1 |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 6 / 58 (10.34%) | 1 / 60 (1.67%) |
| occurrences (all) | 1 | 6 | 1 |
| HYPERKALAEMIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 58 (3.45%) | 2 / 60 (3.33%) |
| occurrences (all) | 0 | 2 | 2 |
| HYPOCALCAEMIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 58 (5.17%) | 2 / 60 (3.33%) |
| occurrences (all) | 0 | 3 | 2 |
| HYPOGLYCAEMIA | | | |

| | | | |
|-----------------------------|-----------------|-----------------|------------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 58 (1.72%) | 0 / 60 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 9 / 58 (15.52%) | 5 / 60 (8.33%) |
| occurrences (all) | 2 | 13 | 5 |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 4 / 14 (28.57%) | 7 / 58 (12.07%) | 10 / 60 (16.67%) |
| occurrences (all) | 5 | 9 | 24 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 7 / 58 (12.07%) | 6 / 60 (10.00%) |
| occurrences (all) | 3 | 7 | 8 |
| HYPOPHOSPHATAEMIA | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 58 (1.72%) | 1 / 60 (1.67%) |
| occurrences (all) | 0 | 1 | 1 |

| | | | |
|---|---|--|--|
| Non-serious adverse events | Phase 2: Placebo + Carboplatin/Etoposide -> Placebo | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 53 / 60 (88.33%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| CANCER PAIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| MALIGNANT NEOPLASM PROGRESSION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| METASTASES TO CENTRAL NERVOUS SYSTEM | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vascular disorders | | | |
| HAEMATOMA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| HOT FLUSH | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| HYPERTENSION | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences (all) | 3 | | |
| HYPOTENSION | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| INTERMITTENT CLAUDICATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 3 | | |
| CHEST PAIN | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| CREPITATIONS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| CRYING | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| FACE OEDEMA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| FATIGUE | | | |
| subjects affected / exposed | 10 / 60 (16.67%) | | |
| occurrences (all) | 12 | | |
| FEELING ABNORMAL | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| FEELING COLD | | | |

| | | | |
|------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| GAIT DISTURBANCE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| INJECTION SITE EXTRAVASATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| INJECTION SITE HAEMATOMA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| INJECTION SITE PHLEBITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| LOSS OF CONTROL OF LEGS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| MALAISE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences (all) | 3 | | |
| NECROSIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 4 / 60 (6.67%) | | |
| occurrences (all) | 4 | | |
| OEDEMA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| OEDEMA PERIPHERAL | | | |

| | | | |
|---|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>5 / 60 (8.33%)</p> <p>5</p> | | |
| <p>PAIN</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 60 (5.00%)</p> <p>3</p> | | |
| <p>PYREXIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>8 / 60 (13.33%)</p> <p>10</p> | | |
| <p>SWELLING</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 60 (0.00%)</p> <p>0</p> | | |
| <p>SWELLING FACE</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 60 (0.00%)</p> <p>0</p> | | |
| <p>Immune system disorders</p> <p>DRUG HYPERSENSITIVITY</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 60 (0.00%)</p> <p>0</p> | | |
| <p>Reproductive system and breast disorders</p> <p>PERINEAL PAIN</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 60 (0.00%)</p> <p>0</p> | | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>ASTHMA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>COUGH</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>DYSPHONIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>DYSPNOEA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>EPISTAXIS</p> | <p>0 / 60 (0.00%)</p> <p>0</p> <p>7 / 60 (11.67%)</p> <p>7</p> <p>1 / 60 (1.67%)</p> <p>1</p> <p>7 / 60 (11.67%)</p> <p>10</p> | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| HAEMOPTYSIS | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences (all) | 3 | | |
| HICCUPS | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| PRODUCTIVE COUGH | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences (all) | 3 | | |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| RHINITIS ALLERGIC | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| RHINORRHOEA | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences (all) | 4 | | |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| CONFUSIONAL STATE | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| DELIRIUM | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| DEPRESSION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---------------------------------------|----------------|--|--|
| HALLUCINATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| INSOMNIA | | | |
| subjects affected / exposed | 4 / 60 (6.67%) | | |
| occurrences (all) | 4 | | |
| RESTLESSNESS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| TENSION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| Product issues | | | |
| DEVICE OCCLUSION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 10 | | |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 3 | | |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 3 | | |
| BLOOD CREATININE INCREASED | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| BLOOD LACTATE DEHYDROGENASE INCREASED | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| GAMMA-GLUTAMYLTRANSFERASE INCREASED | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| HLA MARKER STUDY POSITIVE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| INTERNATIONAL NORMALISED RATIO INCREASED | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| LYMPHOCYTE COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| NEUTROPHIL COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| TRANSAMINASES INCREASED | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| URINE OUTPUT DECREASED | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 7 / 60 (11.67%) | | |
| occurrences (all) | 11 | | |
| WEIGHT INCREASED | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| WHITE BLOOD CELL COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|------------------------------|----------------|--|--|
| CHEMICAL PHLEBITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| FOREARM FRACTURE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| INFUSION RELATED REACTION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| MUSCLE RUPTURE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| MUSCLE STRAIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| POST PROCEDURAL COMPLICATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PROCEDURAL HEADACHE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| SKIN ABRASION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cardiac disorders | | | |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| LEFT VENTRICULAR FAILURE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PALPITATIONS | | | |

| | | | |
|------------------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| ATAXIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| DISTURBANCE IN ATTENTION | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 2 | | |
| DIZZINESS | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences (all) | 4 | | |
| DYSARTHRIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| DYSGEUSIA | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| HEAD DISCOMFORT | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| HEADACHE | | | |
| subjects affected / exposed | 7 / 60 (11.67%) | | |
| occurrences (all) | 7 | | |
| MEMORY IMPAIRMENT | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| MUSCLE CONTRACTIONS INVOLUNTARY | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| NEUROPATHY PERIPHERAL | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PERIPHERAL MOTOR NEUROPATHY | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| POLYNEUROPATHY | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PRESYNCOPE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| SOMNOLENCE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| TREMOR | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 26 / 60 (43.33%) | | |
| occurrences (all) | 55 | | |
| DISSEMINATED INTRAVASCULAR COAGULATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| FEBRILE NEUTROPENIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| LEUKOPENIA | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences (all) | 13 | | |
| NEUTROPENIA | | | |

| | | | |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 28 / 60 (46.67%) | | |
| occurrences (all) | 71 | | |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 12 / 60 (20.00%) | | |
| occurrences (all) | 22 | | |
| Ear and labyrinth disorders | | | |
| EAR DISCOMFORT | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| HYPOACUSIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| OTOTOXICITY | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| TINNITUS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye disorders | | | |
| BLINDNESS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| DRY EYE | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| EYE IRRITATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| EYE PAIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| LACRIMATION INCREASED | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| VITREOUS DETACHMENT | | | |

| | | | |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| ABDOMINAL DISCOMFORT | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| ABDOMINAL DISTENSION | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences (all) | 3 | | |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| ANAL INFLAMMATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| ASCITES | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| CONSTIPATION | | | |
| subjects affected / exposed | 11 / 60 (18.33%) | | |
| occurrences (all) | 15 | | |
| DIARRHOEA | | | |
| subjects affected / exposed | 11 / 60 (18.33%) | | |
| occurrences (all) | 12 | | |
| DIVERTICULUM | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| DRY MOUTH | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| DYSPEPSIA | | | |
| subjects affected / exposed | 4 / 60 (6.67%) | | |
| occurrences (all) | 5 | | |

| | | | |
|------------------------------------|------------------|--|--|
| DYSPHAGIA | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| ENTEROVESICAL FISTULA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| ERUCTATION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| FLATULENCE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| GASTRITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| GASTROESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences (all) | 3 | | |
| HAEMATOCHESIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| HAEMORRHOIDS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| LOWER GASTROINTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| NAUSEA | | | |
| subjects affected / exposed | 21 / 60 (35.00%) | | |
| occurrences (all) | 29 | | |
| ESOPHAGITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| ORAL DISCOMFORT | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PROCTALGIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PROCTITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| RETCHING | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| STOMATITIS | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences (all) | 4 | | |
| VOMITING | | | |
| subjects affected / exposed | 8 / 60 (13.33%) | | |
| occurrences (all) | 9 | | |
| Hepatobiliary disorders | | | |
| HEPATIC PAIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| ALOPECIA | | | |
| subjects affected / exposed | 18 / 60 (30.00%) | | |
| occurrences (all) | 20 | | |
| DRY SKIN | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| ECCHYMOSIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| ECZEMA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| HYPERHIDROSIS | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| NIGHT SWEATS | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| PETECHIAE | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PIGMENTATION DISORDER | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PRURITUS | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| RASH | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| RASH MACULAR | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| SKIN ULCER | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| STICKY SKIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal and urinary disorders | | | |
| DYSURIA | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| NOCTURIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PNEUMATURIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--|----------------------|--|--|
| POST MICTURITION DRIBBLE subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | | |
| TUBULOINTERSTITIAL NEPHRITIS subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | | |
| URINARY HESITATION subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | | |
| URINARY INCONTINENCE subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) 1 | | |
| URINARY RETENTION subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) 1 | | |
| Endocrine disorders INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | | |
| BACK PAIN subjects affected / exposed occurrences (all) | 9 / 60 (15.00%) 9 | | |
| BONE PAIN subjects affected / exposed occurrences (all) | 3 / 60 (5.00%) 3 | | |
| COCCYDYNIA subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | | |
| FLANK PAIN subjects affected / exposed occurrences (all) | 2 / 60 (3.33%) 2 | | |
| GROIN PAIN | | | |

| | | | |
|--------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| INTERVERTEBRAL DISC PROTRUSION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| MUSCULOSKELETAL STIFFNESS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| MYALGIA | | | |
| subjects affected / exposed | 4 / 60 (6.67%) | | |
| occurrences (all) | 4 | | |
| MYOSITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| NECK PAIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| PAIN IN JAW | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|-------------------------------|----------------|--|--|
| SPINAL PAIN | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| TENDON PAIN | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| BRONCHITIS | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| CLOSTRIDIUM DIFFICILE COLITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| CYSTITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| ORAL CANDIDIASIS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| ORAL FUNGAL INFECTION | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| PNEUMONIA | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences (all) | 3 | | |
| RESPIRATORY TRACT INFECTION | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| RHINITIS | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| TOOTH ABSCESS | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | | |
| occurrences (all) | 2 | | |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 14 / 60 (23.33%) | | |
| occurrences (all) | 16 | | |
| DEHYDRATION | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 6 / 60 (10.00%) | | |
| occurrences (all) | 7 | | |
| HYPERKALAEMIA | | | |
| subjects affected / exposed | 3 / 60 (5.00%) | | |
| occurrences (all) | 6 | | |
| HYPOCALCAEMIA | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | | |
| occurrences (all) | 1 | | |
| HYPOGLYCAEMIA | | | |
| subjects affected / exposed | 0 / 60 (0.00%) | | |
| occurrences (all) | 0 | | |
| HYPOKALAEMIA | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 7 / 60 (11.67%) | | |
| occurrences (all) | 8 | | |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 9 / 60 (15.00%) | | |
| occurrences (all) | 12 | | |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 4 / 60 (6.67%) | | |
| occurrences (all) | 5 | | |
| HYPOPHOSPATAEMIA | | | |
| subjects affected / exposed | 5 / 60 (8.33%) | | |
| occurrences (all) | 6 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 04 May 2015 | Allowed any advanced/metastatic solid tumors for which carboplatin/etoposide is appropriate. Changed window for baseline radiographic tumor assessments from 14 days to 21 days. Clarified plan for replacement of subjects in the Phase 1 dose-escalation portion of the study. Updated the statistical analysis for Phase 2 and clarified plan for discontinuation of Phase 2 subjects from treatment vs. study. Added DMC to Phase 2 portion of the study. |
| 30 July 2015 | Clarified enrollment and timing of dose escalations during the Phase 1 portion of the study and allow for additional subjects for safety expansion at the RPTD. Clarified PK sampling schedule. Corrected the time of contraceptive use following the last dose of the study drug. |
| 18 December 2015 | Added additional DLT criteria and updated the total number of subjects in the Phase 1 dose-escalation portion of the study. Updated language around new veliparib dosing schedules. Added language to allow for Phase 2 subjects who discontinued carboplatin and etoposide due to toxicity but not disease progression to transition to monotherapy veliparib or placebo. Updated the length of time that subjects were followed on study to "until disease progression." |
| 14 June 2016 | Increased total number of carboplatin, etoposide and veliparib cycles for Phase 2 subjects. Changed Cycle 5 to Maintenance for Phase 2. Increased total number of subjects and sites. |
| 22 November 2016 | Added veliparib/placebo RPTD of 240 mg BID in a 14-day schedule as the veliparib/placebo dose and schedule for Phase 2 combination therapy. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30327308>