



Clinical trial results:

An International, Phase III, Randomized, Double-Blinded, Placebo-Controlled, Multi-Center Study to Assess the Efficacy of ZD6474 versus Placebo in Subjects with Unresectable Locally Advanced or Metastatic Medullary Thyroid Cancer

Summary

| | |
|--------------------------|--|
| EudraCT number | 2005-005077-29 |
| Trial protocol | DE NL FR BE HU PT SE DK AT IT GB CZ ES |
| Global end of trial date | 26 July 2024 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 |
| This version publication date | 09 August 2025 |
| First version publication date | 09 August 2025 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | D4200C00058 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00410761 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Sanofi-Genzyme Code: LPS14811 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Genzyme Corporation |
| Sponsor organisation address | 50 Binney Street, Cambridge, Massachusetts, United States, 02142 |
| Public contact | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com |
| Scientific contact | Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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 | 26 July 2024 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 26 July 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate an improvement in progression-free survival (PFS) with vandetanib as compared to placebo in participants with unresectable locally advanced or metastatic medullary thyroid carcinoma.

Protection of trial subjects:

Participants were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the participant and considering the local culture. During the course of the trial, participants were provided with individual participant cards indicating the nature of the trial the participant is participating, contact details and any information needed in the event of a medical emergency.

Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 23 November 2006 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Australia: 8 |
| Country: Number of subjects enrolled | Austria: 4 |
| Country: Number of subjects enrolled | Belgium: 9 |
| Country: Number of subjects enrolled | Brazil: 6 |
| Country: Number of subjects enrolled | Canada: 12 |
| Country: Number of subjects enrolled | Czechia: 4 |
| Country: Number of subjects enrolled | Denmark: 5 |
| Country: Number of subjects enrolled | France: 45 |
| Country: Number of subjects enrolled | Germany: 28 |
| Country: Number of subjects enrolled | Hungary: 4 |
| Country: Number of subjects enrolled | India: 6 |
| Country: Number of subjects enrolled | Italy: 38 |
| Country: Number of subjects enrolled | Korea, Republic of: 5 |
| Country: Number of subjects enrolled | Netherlands: 13 |
| Country: Number of subjects enrolled | Poland: 32 |
| Country: Number of subjects enrolled | Portugal: 7 |
| Country: Number of subjects enrolled | Romania: 4 |

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Russian Federation: 8 |
| Country: Number of subjects enrolled | Serbia: 7 |
| Country: Number of subjects enrolled | Spain: 4 |
| Country: Number of subjects enrolled | Sweden: 2 |
| Country: Number of subjects enrolled | Switzerland: 7 |
| Country: Number of subjects enrolled | United States: 73 |
| Worldwide total number of subjects | 331 |
| EEA total number of subjects | 199 |

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) | 262 |
| From 65 to 84 years | 69 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

A total of 331 participants were enrolled in the study. The study was conducted at 60 study sites in 23 countries.

Pre-assignment

Screening details:

First participant enrolled 23 November 2006, last participant enrolled 19 October 2007.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Randomized Treatment Period |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Assessor |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Randomized Treatment Period: Vandetanib 300 mg |

Arm description:

Participants received vandetanib 300 mg orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Vandetanib |
| Investigational medicinal product code | ZD6474 |
| Other name | SAR390530 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Vandetanib 300 mg oral tablet was administered once daily.

| | |
|------------------|--------------------------------------|
| Arm title | Randomized Treatment Period: Placebo |
|------------------|--------------------------------------|

Arm description:

Participants received placebo matched to vandetanib orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.

| | |
|--|--------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo matched to vandetanib oral tablet was administered once daily.

| Number of subjects in period 1 | Randomized Treatment Period: Vandetanib 300 mg | Randomized Treatment Period: Placebo |
|--|--|--------------------------------------|
| Started | 231 | 100 |
| Received Randomized Treatment | 231 | 99 |
| Completed | 14 | 1 |
| Not completed | 217 | 99 |
| Consent withdrawn by subject | 11 | 6 |
| Objective disease progression | 103 | 68 |
| Randomized but did not receive treatment | - | 1 |
| Adverse event, non-fatal | 34 | 3 |
| Unspecified | 69 | 21 |

Period 2

| | |
|------------------------------|-----------------------------|
| Period 2 title | Open-Label Treatment Period |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-------------------------------------|
| Are arms mutually exclusive? | No |
| Arm title | Vandetanib 300 mg/Vandetanib 300 mg |

Arm description:

Participants who received vandetanib 300 mg during the blinded randomized treatment period and who were unblinded due to disease progression or as a result of protocol amendment 6 were given the option to continue to receive vandetanib 300 mg orally once daily in the open-label treatment period for as long as they still benefitted of it per investigator judgement or until they were given another anti-cancer therapy.

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Vandetanib |
| Investigational medicinal product code | ZD6474 |
| Other name | SAR390530 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Vandetanib 300 mg oral tablet was administered once daily.

| | |
|------------------|---------------------------|
| Arm title | Placebo/Vandetanib 300 mg |
|------------------|---------------------------|

Arm description:

Participants who received placebo matched to vandetanib during the blinded randomized treatment period and who were unblinded due to disease progression or as a result of protocol amendment 6 were given the option to receive vandetanib 300 mg orally once daily in the open-label treatment period for as long as they still benefitted of it per investigator judgement or until they were given another anti-cancer therapy.

| | |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

| | |
|--|--------------------|
| Investigational medicinal product name | Vandetanib |
| Investigational medicinal product code | ZD6474 |
| Other name | SAR390530 |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Vandetanib 300 mg oral tablet was administered once daily.

| Number of subjects in period 2 | Vandetanib 300 mg/Vandetanib 300 mg | Placebo/Vandetanib 300 mg |
|---------------------------------------|-------------------------------------|---------------------------|
| Started | 109 | 79 |
| Completed | 28 | 21 |
| Not completed | 81 | 58 |
| Consent withdrawn by subject | 8 | 7 |
| Objective disease progression | 42 | 27 |
| Adverse event, non-fatal | 13 | 15 |
| Unspecified | 18 | 9 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Randomized Treatment Period: Vandetanib 300 mg |
|-----------------------|--|

Reporting group description:

Participants received vandetanib 300 mg orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Randomized Treatment Period: Placebo |
|-----------------------|--------------------------------------|

Reporting group description:

Participants received placebo matched to vandetanib orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.

| Reporting group values | Randomized Treatment Period: Vandetanib 300 mg | Randomized Treatment Period: Placebo | Total |
|------------------------------------|--|--------------------------------------|-------|
| Number of subjects | 231 | 100 | 331 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|------------------|------------------|-----|
| Age continuous Units: years arithmetic mean full range (min-max) | 50.7 18 to 83 | 53.4 26 to 84 | - |
| Gender categorical Units: Subjects | | | |
| Female | 97 | 44 | 141 |
| Male | 134 | 56 | 190 |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | Randomized Treatment Period: Vandetanib 300 mg |
| Reporting group description: Participants received vandetanib 300 mg orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period. | |
| Reporting group title | Randomized Treatment Period: Placebo |
| Reporting group description: Participants received placebo matched to vandetanib orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period. | |
| Reporting group title | Vandetanib 300 mg/Vandetanib 300 mg |
| Reporting group description: Participants who received vandetanib 300 mg during the blinded randomized treatment period and who were unblinded due to disease progression or as a result of protocol amendment 6 were given the option to continue to receive vandetanib 300 mg orally once daily in the open-label treatment period for as long as they still benefitted of it per investigator judgement or until they were given another anti-cancer therapy. | |
| Reporting group title | Placebo/Vandetanib 300 mg |
| Reporting group description: Participants who received placebo matched to vandetanib during the blinded randomized treatment period and who were unblinded due to disease progression or as a result of protocol amendment 6 were given the option to receive vandetanib 300 mg orally once daily in the open-label treatment period for as long as they still benefitted of it per investigator judgement or until they were given another anti-cancer therapy. | |

Primary: Progression-Free Survival

| | |
|--|--|
| End point title | Progression-Free Survival ^[1] |
| End point description: Median time to progression (months) from randomisation until objective disease progression (determined by RECIST assessments) or death (by any cause in the absence of objective progression) provided death is within 3 months from the last evaluable RECIST assessment. Values here are estimated (from a Weibull model) as the medians were not met. -99999/99999 indicates that PFS is a time to event endpoint and because the medians were not met in this study there is no appropriate measure of dispersion of the median. | |
| End point type | Primary |
| End point timeframe: RECIST tumour assessments were performed at screening (within 3 weeks before date of randomisation), then once every 12 weeks up to and including discontinuation of blinded study treatment, unless patients had withdrawn consent. | |
| 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: As the endpoint is descriptive in nature, no statistical analysis is provided. | |

| End point values | Randomized Treatment Period: Vandetanib 300 mg | Randomized Treatment Period: Placebo | | |
|-----------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 231 | 100 | | |
| Units: Months | | | | |

| | | | | |
|----------------------------------|------------------------|------------------------|--|--|
| median (confidence interval 95%) | 30.5 (-99999 to 99999) | 19.2 (-99999 to 99999) | | |
|----------------------------------|------------------------|------------------------|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

| | |
|-----------------|-------------------------------|
| End point title | Objective Response Rate (ORR) |
|-----------------|-------------------------------|

End point description:

The ORR is the number of patients that are responders i.e. those patients with a confirmed best objective response of complete response (CR) or partial response (PR) as defined by RECIST criteria. The categories for best objective response are CR, PR, stable disease (SD) \geq 12 weeks, progressive disease (PD) or NE.

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

End point timeframe:

RECIST assessments performed at screening (within 3 weeks before randomisation), then every 12 weeks. For patients with objective response of CR or PR, an additional confirmatory scan was performed \geq 4 weeks following the date of first response.

| End point values | Randomized Treatment Period: Vandetanib 300 mg | Randomized Treatment Period: Placebo | | |
|-----------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 231 | 100 | | |
| Units: Participants | | | | |
| number (not applicable) | 104 | 13 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

| | |
|-----------------|----------------------------|
| End point title | Disease Control Rate (DCR) |
|-----------------|----------------------------|

End point description:

Disease control rate is defined as the number of patients who achieved disease control at 8 weeks following randomisation. Disease control at 8 weeks is defined as a best objective response of complete response (CR), partial response (PR) or stable disease (SD) \geq 12 weeks.

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

End point timeframe:

RECIST tumour assessments were performed at screening (within 3 weeks before date of randomisation), then once every 12 weeks up to and including discontinuation of blinded study treatment, unless patients had withdrawn consent

| End point values | Randomized Treatment Period: Vandetanib 300 mg | Randomized Treatment Period: Placebo | | |
|-----------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 231 | 100 | | |
| Units: Participants | | | | |
| number (not applicable) | 200 | 71 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

| | |
|-----------------|----------------------------|
| End point title | Duration of Response (DoR) |
|-----------------|----------------------------|

End point description:

Response is defined as a confirmed best objective response of CR or PR. Duration of response is defined as time from the date of first documented response until date of documented progression or death in the absence of disease progression (provided death is within 3 months of last RECIST assessment). Values are estimated as the medians weren't met. -99999/99999 indicates that DoR is a time to event endpoint and because the medians were not met in this study there is no appropriate measure of dispersion of the median.

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

End point timeframe:

RECIST tumour assessments were performed at screening (within 3 weeks before date of randomisation), then once every 12 weeks up to and including discontinuation of blinded study treatment, unless patients had withdrawn consent

| End point values | Randomized Treatment Period: Vandetanib 300 mg | Randomized Treatment Period: Placebo | | |
|----------------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 104 | 13 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 22.2 (-99999 to 99999) | 16.3 (-99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

| | |
|-----------------|-----------------------|
| End point title | Overall Survival (OS) |
|-----------------|-----------------------|

End point description:

As data was immature at data cut off, number of death events is quoted.

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

End point timeframe:

Number of deaths since randomisation

| End point values | Randomized Treatment Period: Vandetanib 300 mg | Randomized Treatment Period: Placebo | | |
|-----------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 231 | 100 | | |
| Units: Participants | | | | |
| number (not applicable) | 32 | 16 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Biochemical Response Calcitonin (CTN)

| | |
|-----------------|---------------------------------------|
| End point title | Biochemical Response Calcitonin (CTN) |
|-----------------|---------------------------------------|

End point description:

Best biochemical response was calculated from assessments at baseline and during treatment. Responders were those patients with a best biochemical response of CR or PR, confirmed by repeat assessments, which were to be performed no less than 4 weeks after the criteria for PR or CR were first met. CR and PR being defined according to level of CTN.

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

End point timeframe:

Blood samples Blood samples for analysis of CTN were taken at screening baseline (average of 0, 1, 4 and 8 hours), then every 4 weeks until discontinuation and 60 day follow up

| End point values | Randomized Treatment Period: Vandetanib 300 mg | Randomized Treatment Period: Placebo | | |
|-----------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 231 | 100 | | |
| Units: Participants | | | | |
| number (not applicable) | 160 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Biochemical Response Carcinoembryonic Antigen (CEA)

| | |
|-----------------|---|
| End point title | Biochemical Response Carcinoembryonic Antigen (CEA) |
|-----------------|---|

End point description:

Best biochemical response was calculated from assessments at baseline and during treatment. Responders were those patients with a best biochemical response of CR or PR, confirmed by repeat assessments, which were to be performed no less than 4 weeks after the criteria for PR or CR were first met. CR and PR being defined according to level of CEA.

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

End point timeframe:

Blood samples for analysis of CEA were taken at screening baseline (average of 0, 1, 4 and 8 hours), then every 4 weeks until discontinuation and 60 day follow up

| End point values | Randomized Treatment Period: Vandetanib 300 mg | Randomized Treatment Period: Placebo | | |
|-----------------------------|--|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 231 | 100 | | |
| Units: Participants | | | | |
| number (not applicable) | 119 | 2 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Worsening of Pain (TWP)

| | |
|-----------------|---------------------------------|
| End point title | Time to Worsening of Pain (TWP) |
|-----------------|---------------------------------|

End point description:

TWP was derived using the worst pain score from brief pain inventory (BPI) and patient reported opioid analgesic use. BPI uses 0 to 10 numeric rating scales asking subjects to rate their pain.

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

End point timeframe:

During the last week of the screening period (Day -7 to Day 0), the brief pain inventory (BPI) and opioid analgesic use were self-reported once a day for 4 days to establish baseline, then every week during blinded study treatment, up to discontinuation.

| End point values | Randomized Treatment Period: Vandetanib 300 mg | Randomized Treatment Period: Placebo | | |
|-----------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 231 | 100 | | |
| Units: Weeks | | | | |
| number (not applicable) | 7.8 | 3.3 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and deaths: From randomization (Day 1) up to end of follow-up, approximately 212 months. Non-serious adverse events: From randomization (Day 1) up to data cut-off date of 01-Jun-2010, approximately 42 months.

Adverse event reporting additional description:

The safety population included all participants who received at least 1 dose of vandetanib/placebo. AEs and SAEs were collected from Day 1 to cut-off date 01-Jun-2010 and were presented in clinical database. After this cut-off date, SAEs were reported in pharmacovigilance database, but no non-serious AEs were reported.

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

Dictionary used

| | |
|--------------------|-----------|
| Dictionary name | MedDRA |
| Dictionary version | 13 - 25.1 |

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Randomized Treatment Period: Vandetanib 300 mg |
|-----------------------|--|

Reporting group description:

Participants received vandetanib 300 mg orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Randomized Treatment Period: Placebo |
|-----------------------|--------------------------------------|

Reporting group description:

Participants received placebo matched to vandetanib orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.

| | |
|-----------------------|---|
| Reporting group title | Open-Label Treatment Period: Vandetanib 300 mg/Vandetanib 300 |
|-----------------------|---|

Reporting group description:

Participants who received vandetanib 300 mg during the blinded randomized treatment period and who were unblinded due to disease progression or as a result of protocol amendment 6 were given the option to continue to receive vandetanib 300 mg orally once daily in the open-label treatment period for as long as they still benefitted of it per investigator judgement or until they were given another anti-cancer therapy.

| | |
|-----------------------|--|
| Reporting group title | Open-Label Treatment Period: Placebo/Vandetanib 300 mg |
|-----------------------|--|

Reporting group description:

Participants who received placebo matched to vandetanib during the blinded randomized treatment period and who were unblinded due to disease progression or as a result of protocol amendment 6 were given the option to receive vandetanib 300 mg orally once daily in the open-label treatment period for as long as they still benefitted of it per investigator judgement or until they were given another anti-cancer therapy.

| Serious adverse events | Randomized Treatment Period: Vandetanib 300 mg | Randomized Treatment Period: Placebo | Open-Label Treatment Period: Vandetanib 300 mg/Vandetanib 300 |
|---|--|--------------------------------------|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 92 / 231 (39.83%) | 16 / 99 (16.16%) | 53 / 109 (48.62%) |
| number of deaths (all causes) | 66 | 10 | 52 |
| number of deaths resulting from adverse events | 10 | 2 | 7 |

| | | | |
|---|-----------------|----------------|-----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast Cancer Female | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Basal Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 Myeloid Leukaemia | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colorectal Adenoma | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung Neoplasm Malignant | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| 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 Bone | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Germ Cell Cancer | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Hepatic Cancer Metastatic | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |

| | | | |
|---|-----------------|----------------|-----------------|
| Pancreatic Neoplasm | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Prostate Cancer | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Phaeochromocytoma | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 |
| Squamous Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous Cell Carcinoma Of Skin | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Testicular Seminoma (Pure) | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Accelerated Hypertension | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Deep Vein Thrombosis | | | |

| | | | |
|--|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertensive Crisis | | | |
| subjects affected / exposed | 4 / 231 (1.73%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |
| subjects affected / exposed | 3 / 231 (1.30%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 3 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Jugular Vein Thrombosis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Pelvic Venous Thrombosis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion Spontaneous | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| Asthenia | | | |
| subjects affected / exposed | 2 / 231 (0.87%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device Occlusion | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Chest Pain | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 2 / 109 (1.83%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 1 / 99 (1.01%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General Physical Health Deterioration | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 1 / 99 (1.01%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mucosal Inflammation | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden Death | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Swelling | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Iodine Allergy | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 |
| Reproductive system and breast disorders | | | |
| Intermenstrual Bleeding | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ovarian Cyst Ruptured | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthmatic Crisis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute Respiratory Distress Syndrome | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchospasm | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Chylothorax | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Cough | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 1 / 99 (1.01%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Interstitial Lung Disease | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung Disorder | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung Infiltration | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| 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 Effusion | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 Aspiration | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Pneumonitis | | | |
| subjects affected / exposed | 2 / 231 (0.87%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary Embolism | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary Oedema | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary Thrombosis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 |
| Respiratory Arrest | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Respiratory Failure | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bipolar Disorder | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Depression | | | |
| subjects affected / exposed | 3 / 231 (1.30%) | 0 / 99 (0.00%) | 2 / 109 (1.83%) |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Confusional State | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Completed Suicide | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide Attempt | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| Blood Creatine Phosphokinase Increased | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| 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 Creatinine Increased | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| C-Reactive Protein Increased | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Electrocardiogram Qt Prolonged | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Hepatic Enzyme Increased | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| International Normalised Ratio Increased | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Prostatic Specific Antigen Increased | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 | | | |
| Compression Fracture | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Exposure During Pregnancy | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Jaw Fracture | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 |
| Joint Injury | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Overdose | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 |
| Post Procedural Complication | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Post Procedural Haematuria | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Road Traffic Accident | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seroma | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Spinal Compression Fracture | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 |
| Spinal Fracture | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Tibia Fracture | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Venomous Bite | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Wound Dehiscence | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound Necrosis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Patent Ductus Arteriosus | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| 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 disorders | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| Acute Myocardial Infarction | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 4 / 109 (3.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| Arrhythmia | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Atrial Fibrillation | | | |
| subjects affected / exposed | 2 / 231 (0.87%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bradycardia | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Cardiac Failure Acute | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Cardiac Failure Congestive | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| 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 | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Cardiovascular Insufficiency | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Myocardial Infarction | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Pericardial Effusion | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial Haemorrhage | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Stress Cardiomyopathy | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Brain Oedema | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Carotid Artery Stenosis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebellar Syndrome | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral Ischaemia | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 3 / 109 (2.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Convulsion | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Depressed Level Of Consciousness | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 3 / 109 (2.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 |
| Internal Capsule Infarction | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loss Of Consciousness | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 3 / 231 (1.30%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 0 / 109 (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 |
| Peripheral Sensorimotor Neuropathy | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Somnolence | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Spinal Cord Compression | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subarachnoid Haemorrhage | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 1 / 99 (1.01%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient Ischaemic Attack | | | |
| subjects affected / exposed | 2 / 231 (0.87%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disseminated Intravascular Coagulation | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Glaucoma | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Retinal Artery Occlusion | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal Detachment | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vision Blurred | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 4 / 231 (1.73%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Diarrhoea | | | |
| subjects affected / exposed | 6 / 231 (2.60%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 4 / 6 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dry Mouth | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| 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 | 2 / 231 (0.87%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Faecaloma | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal Haemorrhage | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 1 / 99 (1.01%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Gastrointestinal Inflammation | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Intestinal Obstruction | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| 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 Perforation | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mechanical Ileus | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive Pancreatitis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| 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 | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis Acute | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 3 / 109 (2.75%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis Chronic | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis Haemorrhagic | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Pneumatosis Intestinalis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Rectal Haemorrhage | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Reflux Gastritis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small Intestinal Perforation | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Subileus | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| 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 | 2 / 231 (0.87%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Biliary Colic | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 2 / 109 (1.83%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis | | | |
| subjects affected / exposed | 2 / 231 (0.87%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis Acute | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholestasis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatitis Acneiform | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Photosensitivity Reaction | | | |
| subjects affected / exposed | 2 / 231 (0.87%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Rash | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Skin Exfoliation | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin Ulcer | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| Anuria | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Calculus Ureteric | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Calculus Urinary | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| 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 Kidney Disease | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive Uropathy | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 3 / 231 (1.30%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal Colic | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal Failure | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal Failure Acute | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Tubulointerstitial Nephritis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Endocrine disorders | | | |
| Cushing's Syndrome | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| 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 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back Pain | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 2 / 109 (1.83%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone Pain | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|-----------------|
| Flank Pain | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal Chest Pain | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myopathy | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neck Pain | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal Abscess | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal Wall Abscess | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Appendicitis | | | |
| subjects affected / exposed | 3 / 231 (1.30%) | 0 / 99 (0.00%) | 3 / 109 (2.75%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis Perforated | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bartholin's Abscess | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary Sepsis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| 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 | 2 / 231 (0.87%) | 1 / 99 (1.01%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis Bacterial | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Covid-19 | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatitis Infected | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 2 / 231 (0.87%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Folliculitis | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 1 / 99 (1.01%) | 2 / 109 (1.83%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Gastroenteritis Bacterial | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Gastroenteritis Viral | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal Infection | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Infected Bites | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Infection | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngitis | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower Respiratory Tract Infection | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung Infection | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Meningitis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningitis Bacterial | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peridiverticular Abscess | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 7 / 231 (3.03%) | 0 / 99 (0.00%) | 3 / 109 (2.75%) |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 0 | 1 / 5 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Postoperative Wound Infection | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory Tract Infection | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal Infection | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Sepsis | | | |
| subjects affected / exposed | 4 / 231 (1.73%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Staphylococcal Sepsis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Streptococcal Sepsis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tracheitis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary Tract Infection | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 3 / 231 (1.30%) | 0 / 99 (0.00%) | 2 / 109 (1.83%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary Tract Infection Pseudomonal | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 2 / 109 (1.83%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Acidosis | | | |
| subjects affected / exposed | 0 / 231 (0.00%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Decreased Appetite | | | |
| subjects affected / exposed | 4 / 231 (1.73%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 3 / 231 (1.30%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes Mellitus | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 1 / 99 (1.01%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 3 / 231 (1.30%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypocalcaemia | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 2 / 231 (0.87%) | 0 / 99 (0.00%) | 2 / 109 (1.83%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 2 / 231 (0.87%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 231 (0.87%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Ketoacidosis | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 |
| Malnutrition | | | |
| subjects affected / exposed | 1 / 231 (0.43%) | 0 / 99 (0.00%) | 0 / 109 (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 | Open-Label Treatment Period: Placebo/Vandetanib 300 mg | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 36 / 79 (45.57%) | | |
| number of deaths (all causes) | 41 | | |
| number of deaths resulting from adverse events | 3 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Breast Cancer Female | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Basal Cell Carcinoma | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 9 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chronic Myeloid Leukaemia | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colorectal Adenoma | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung Neoplasm Malignant | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metastases To Bone | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Germ Cell Cancer | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic Cancer Metastatic | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatic Neoplasm | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostate Cancer | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Phaeochromocytoma | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Squamous Cell Carcinoma | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal Cell Carcinoma | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Squamous Cell Carcinoma Of Skin | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Testicular Seminoma (Pure) | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Accelerated Hypertension | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Deep Vein Thrombosis | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertensive Crisis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Jugular Vein Thrombosis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vena Cava Thrombosis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pelvic Venous Thrombosis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion Spontaneous | | | |
| subjects affected / exposed | 0 / 79 (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 | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Device Occlusion | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chest Pain | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fatigue | | | | |
| subjects affected / exposed | 0 / 79 (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 | 2 / 79 (2.53%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Malaise | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mucosal Inflammation | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyrexia | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sudden Death | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Swelling | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Iodine Allergy | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Intermenstrual Bleeding | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ovarian Cyst Ruptured | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthmatic Crisis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute Respiratory Distress Syndrome | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchospasm | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chylothorax | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Epistaxis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dyspnoea | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cough | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemoptysis | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Interstitial Lung Disease | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung Disorder | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung Infiltration | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pleural Effusion | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia Aspiration | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonitis | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumothorax | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary Embolism | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary Oedema | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary Thrombosis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory Arrest | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory Failure | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bipolar Disorder | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Depression | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Confusional State | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Completed Suicide | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Suicide Attempt | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |

| | | | | |
|---|----------------|--|--|--|
| Blood Creatine Phosphokinase Increased | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood Creatinine Increased | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| C-Reactive Protein Increased | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Electrocardiogram Qt Prolonged | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic Enzyme Increased | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| International Normalised Ratio Increased | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Prostatic Specific Antigen Increased | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Injury, poisoning and procedural complications | | | | |
| Compression Fracture | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Exposure During Pregnancy | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Jaw Fracture | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint Injury | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Overdose | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post Procedural Complication | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post Procedural Haematuria | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Road Traffic Accident | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Seroma | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal Compression Fracture | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal Fracture | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tibia Fracture | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Venomous Bite | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound Dehiscence | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound Necrosis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic disorders | | | |
| Patent Ductus Arteriosus | | | |
| subjects affected / exposed | 0 / 79 (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 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arrhythmia | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial Fibrillation | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bradycardia | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac Failure Acute | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac Failure Congestive | | | | |
| subjects affected / exposed | 0 / 79 (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 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiovascular Insufficiency | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myocardial Infarction | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pericardial Effusion | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pericardial Haemorrhage | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stress Cardiomyopathy | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Brain Oedema | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Carotid Artery Stenosis | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebellar Syndrome | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral Ischaemia | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cerebrovascular Accident | | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Convulsion | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Depressed Level Of Consciousness | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dizziness | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Epilepsy | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hemiparesis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Internal Capsule Infarction | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Loss Of Consciousness | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral Sensorimotor Neuropathy | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Somnolence | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal Cord Compression | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subarachnoid Haemorrhage | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transient Ischaemic Attack | | | |
| subjects affected / exposed | 0 / 79 (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 | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Disseminated Intravascular Coagulation | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Glaucoma | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Retinal Artery Occlusion | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Retinal Detachment | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vision Blurred | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal Pain | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dry Mouth | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Faecaloma | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal Haemorrhage | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal Inflammation | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ileus | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal Obstruction | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal Perforation | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mechanical Ileus | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Obstructive Pancreatitis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nausea | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatitis Acute | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis Chronic | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis Haemorrhagic | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumatosis Intestinalis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rectal Haemorrhage | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reflux Gastritis | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small Intestinal Perforation | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subileus | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Biliary Colic | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis Acute | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholestasis | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Jaundice | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dermatitis Acneiform | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Photosensitivity Reaction | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rash | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin Exfoliation | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin Ulcer | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |

| | | | | |
|---|----------------|--|--|--|
| Anuria | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Calculus Ureteric | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Calculus Urinary | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chronic Kidney Disease | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hydronephrosis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Obstructive Uropathy | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nephrolithiasis | | | | |
| subjects affected / exposed | 3 / 79 (3.80%) | | | |
| occurrences causally related to treatment / all | 1 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal Colic | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal Failure | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 2 / 79 (2.53%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal Failure Acute | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tubulointerstitial Nephritis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| Cushing's Syndrome | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Back Pain | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bone Pain | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Flank Pain | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Musculoskeletal Chest Pain | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myopathy | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neck Pain | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteoarthritis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infections and infestations | | | | |
| Abdominal Abscess | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal Wall Abscess | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Appendicitis | | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Appendicitis Perforated | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bartholin's Abscess | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Biliary Sepsis | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Bronchitis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchitis Bacterial | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Covid-19 | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dermatitis Infected | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Folliculitis | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis Bacterial | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis Viral | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal Infection | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infected Bites | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infection | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Influenza | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Laryngitis | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower Respiratory Tract Infection | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung Infection | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meningitis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meningitis Bacterial | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peridiverticular Abscess | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritonitis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Postoperative Wound Infection | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyelonephritis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory Tract Infection | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Staphylococcal Infection | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Staphylococcal Sepsis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Streptococcal Sepsis | | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tracheitis | | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary Tract Infection | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary Tract Infection Pseudomonal | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Acidosis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Decreased Appetite | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dehydration | | | |
| subjects affected / exposed | 3 / 79 (3.80%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetes Mellitus | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypocalcaemia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 79 (1.27%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ketoacidosis | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 79 (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 | Randomized Treatment Period: Vandetanib 300 mg | Randomized Treatment Period: Placebo | Open-Label Treatment Period: Vandetanib 300 mg/Vandetanib 300 |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 226 / 231 (97.84%) | 87 / 99 (87.88%) | 32 / 109 (29.36%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 71 / 231 (30.74%) | 6 / 99 (6.06%) | 2 / 109 (1.83%) |
| occurrences (all) | 79 | 6 | 2 |

| | | | |
|--|-------------------|------------------|-----------------|
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 34 / 231 (14.72%) | 12 / 99 (12.12%) | 0 / 109 (0.00%) |
| occurrences (all) | 39 | 12 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 54 / 231 (23.38%) | 23 / 99 (23.23%) | 3 / 109 (2.75%) |
| occurrences (all) | 64 | 27 | 3 |
| Pyrexia | | | |
| subjects affected / exposed | 18 / 231 (7.79%) | 3 / 99 (3.03%) | 3 / 109 (2.75%) |
| occurrences (all) | 20 | 3 | 3 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 28 / 231 (12.12%) | 10 / 99 (10.10%) | 3 / 109 (2.75%) |
| occurrences (all) | 31 | 15 | 3 |
| Dysphonia | | | |
| subjects affected / exposed | 17 / 231 (7.36%) | 3 / 99 (3.03%) | 1 / 109 (0.92%) |
| occurrences (all) | 18 | 3 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 16 / 231 (6.93%) | 10 / 99 (10.10%) | 3 / 109 (2.75%) |
| occurrences (all) | 17 | 14 | 4 |
| Dyspnoea Exertional | | | |
| subjects affected / exposed | 3 / 231 (1.30%) | 5 / 99 (5.05%) | 0 / 109 (0.00%) |
| occurrences (all) | 3 | 5 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 18 / 231 (7.79%) | 5 / 99 (5.05%) | 0 / 109 (0.00%) |
| occurrences (all) | 20 | 6 | 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 6 / 231 (2.60%) | 1 / 99 (1.01%) | 0 / 109 (0.00%) |
| occurrences (all) | 6 | 1 | 0 |
| Oropharyngeal Pain | | | |
| subjects affected / exposed | 20 / 231 (8.66%) | 6 / 99 (6.06%) | 1 / 109 (0.92%) |
| occurrences (all) | 32 | 14 | 1 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 12 / 231 (5.19%) | 5 / 99 (5.05%) | 0 / 109 (0.00%) |
| occurrences (all) | 13 | 5 | 0 |

| | | | |
|--|--------------------------|------------------------|----------------------|
| Depression subjects affected / exposed occurrences (all) | 22 / 231 (9.52%) 25 | 3 / 99 (3.03%) 3 | 1 / 109 (0.92%) 1 |
| Insomnia subjects affected / exposed occurrences (all) | 32 / 231 (13.85%) 36 | 12 / 99 (12.12%) 12 | 1 / 109 (0.92%) 1 |
| Investigations Electrocardiogram Qt Prolonged subjects affected / exposed occurrences (all) | 32 / 231 (13.85%) 46 | 1 / 99 (1.01%) 1 | 3 / 109 (2.75%) 3 |
| Weight Increased subjects affected / exposed occurrences (all) | 6 / 231 (2.60%) 6 | 0 / 99 (0.00%) 0 | 0 / 109 (0.00%) 0 |
| Weight Decreased subjects affected / exposed occurrences (all) | 27 / 231 (11.69%) 28 | 10 / 99 (10.10%) 10 | 2 / 109 (1.83%) 2 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 21 / 231 (9.09%) 24 | 5 / 99 (5.05%) 5 | 1 / 109 (0.92%) 1 |
| Dysgeusia subjects affected / exposed occurrences (all) | 20 / 231 (8.66%) 22 | 3 / 99 (3.03%) 3 | 0 / 109 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 62 / 231 (26.84%) 138 | 9 / 99 (9.09%) 13 | 4 / 109 (3.67%) 6 |
| Paraesthesia subjects affected / exposed occurrences (all) | 13 / 231 (5.63%) 15 | 3 / 99 (3.03%) 3 | 2 / 109 (1.83%) 4 |
| Tremor subjects affected / exposed occurrences (all) | 7 / 231 (3.03%) 7 | 0 / 99 (0.00%) 0 | 1 / 109 (0.92%) 1 |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 10 / 231 (4.33%) 12 | 2 / 99 (2.02%) 2 | 1 / 109 (0.92%) 1 |
| Eye disorders | | | |

| | | | |
|--|---------------------------|------------------------|----------------------|
| Corneal Opacity subjects affected / exposed occurrences (all) | 11 / 231 (4.76%) 11 | 0 / 99 (0.00%) 0 | 0 / 109 (0.00%) 0 |
| Vision Blurred subjects affected / exposed occurrences (all) | 19 / 231 (8.23%) 23 | 1 / 99 (1.01%) 1 | 1 / 109 (0.92%) 1 |
| Gastrointestinal disorders | | | |
| Abdominal Pain subjects affected / exposed occurrences (all) | 33 / 231 (14.29%) 50 | 5 / 99 (5.05%) 6 | 2 / 109 (1.83%) 2 |
| Abdominal Pain Upper subjects affected / exposed occurrences (all) | 23 / 231 (9.96%) 33 | 7 / 99 (7.07%) 7 | 1 / 109 (0.92%) 1 |
| Constipation subjects affected / exposed occurrences (all) | 14 / 231 (6.06%) 21 | 5 / 99 (5.05%) 5 | 3 / 109 (2.75%) 3 |
| Diarrhoea subjects affected / exposed occurrences (all) | 123 / 231 (53.25%) 180 | 27 / 99 (27.27%) 36 | 4 / 109 (3.67%) 5 |
| Dry Mouth subjects affected / exposed occurrences (all) | 22 / 231 (9.52%) 22 | 3 / 99 (3.03%) 3 | 0 / 109 (0.00%) 0 |
| Toothache subjects affected / exposed occurrences (all) | 7 / 231 (3.03%) 7 | 5 / 99 (5.05%) 17 | 2 / 109 (1.83%) 2 |
| Nausea subjects affected / exposed occurrences (all) | 74 / 231 (32.03%) 97 | 16 / 99 (16.16%) 16 | 5 / 109 (4.59%) 5 |
| Dyspepsia subjects affected / exposed occurrences (all) | 28 / 231 (12.12%) 33 | 4 / 99 (4.04%) 5 | 1 / 109 (0.92%) 1 |
| Vomiting subjects affected / exposed occurrences (all) | 33 / 231 (14.29%) 45 | 7 / 99 (7.07%) 7 | 3 / 109 (2.75%) 5 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|--------------------|------------------|-----------------|
| Acne | | | |
| subjects affected / exposed | 47 / 231 (20.35%) | 5 / 99 (5.05%) | 0 / 109 (0.00%) |
| occurrences (all) | 66 | 5 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 18 / 231 (7.79%) | 0 / 99 (0.00%) | 2 / 109 (1.83%) |
| occurrences (all) | 19 | 0 | 2 |
| Dermatitis Acneiform | | | |
| subjects affected / exposed | 35 / 231 (15.15%) | 2 / 99 (2.02%) | 0 / 109 (0.00%) |
| occurrences (all) | 45 | 4 | 0 |
| Dry Skin | | | |
| subjects affected / exposed | 36 / 231 (15.58%) | 5 / 99 (5.05%) | 0 / 109 (0.00%) |
| occurrences (all) | 41 | 5 | 0 |
| Erythema | | | |
| subjects affected / exposed | 22 / 231 (9.52%) | 3 / 99 (3.03%) | 0 / 109 (0.00%) |
| occurrences (all) | 22 | 3 | 0 |
| Rash | | | |
| subjects affected / exposed | 105 / 231 (45.45%) | 11 / 99 (11.11%) | 4 / 109 (3.67%) |
| occurrences (all) | 158 | 12 | 4 |
| Pruritus | | | |
| subjects affected / exposed | 26 / 231 (11.26%) | 4 / 99 (4.04%) | 0 / 109 (0.00%) |
| occurrences (all) | 31 | 5 | 0 |
| Photosensitivity Reaction | | | |
| subjects affected / exposed | 29 / 231 (12.55%) | 0 / 99 (0.00%) | 0 / 109 (0.00%) |
| occurrences (all) | 33 | 0 | 0 |
| Renal and urinary disorders | | | |
| Proteinuria | | | |
| subjects affected / exposed | 23 / 231 (9.96%) | 2 / 99 (2.02%) | 1 / 109 (0.92%) |
| occurrences (all) | 26 | 3 | 1 |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 16 / 231 (6.93%) | 0 / 99 (0.00%) | 1 / 109 (0.92%) |
| occurrences (all) | 19 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 19 / 231 (8.23%) | 10 / 99 (10.10%) | 2 / 109 (1.83%) |
| occurrences (all) | 24 | 13 | 2 |

| | | | |
|-----------------------------------|-------------------|------------------|-----------------|
| Back Pain | | | |
| subjects affected / exposed | 23 / 231 (9.96%) | 20 / 99 (20.20%) | 6 / 109 (5.50%) |
| occurrences (all) | 37 | 41 | 9 |
| Bone Pain | | | |
| subjects affected / exposed | 10 / 231 (4.33%) | 5 / 99 (5.05%) | 0 / 109 (0.00%) |
| occurrences (all) | 10 | 5 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 10 / 231 (4.33%) | 2 / 99 (2.02%) | 2 / 109 (1.83%) |
| occurrences (all) | 11 | 2 | 2 |
| Musculoskeletal Pain | | | |
| subjects affected / exposed | 12 / 231 (5.19%) | 10 / 99 (10.10%) | 3 / 109 (2.75%) |
| occurrences (all) | 20 | 14 | 3 |
| Musculoskeletal Chest Pain | | | |
| subjects affected / exposed | 18 / 231 (7.79%) | 6 / 99 (6.06%) | 2 / 109 (1.83%) |
| occurrences (all) | 24 | 7 | 2 |
| Muscle Spasms | | | |
| subjects affected / exposed | 14 / 231 (6.06%) | 1 / 99 (1.01%) | 0 / 109 (0.00%) |
| occurrences (all) | 16 | 2 | 0 |
| Neck Pain | | | |
| subjects affected / exposed | 17 / 231 (7.36%) | 9 / 99 (9.09%) | 0 / 109 (0.00%) |
| occurrences (all) | 20 | 10 | 0 |
| Pain In Extremity | | | |
| subjects affected / exposed | 17 / 231 (7.36%) | 14 / 99 (14.14%) | 3 / 109 (2.75%) |
| occurrences (all) | 24 | 17 | 3 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 11 / 231 (4.76%) | 6 / 99 (6.06%) | 0 / 109 (0.00%) |
| occurrences (all) | 11 | 8 | 0 |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 19 / 231 (8.23%) | 3 / 99 (3.03%) | 2 / 109 (1.83%) |
| occurrences (all) | 27 | 5 | 2 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 29 / 231 (12.55%) | 9 / 99 (9.09%) | 2 / 109 (1.83%) |
| occurrences (all) | 43 | 12 | 4 |
| Influenza | | | |

| | | | |
|--|-------------------------|------------------------|----------------------|
| subjects affected / exposed occurrences (all) | 16 / 231 (6.93%) 16 | 3 / 99 (3.03%) 3 | 2 / 109 (1.83%) 2 |
| Folliculitis subjects affected / exposed occurrences (all) | 8 / 231 (3.46%) 9 | 1 / 99 (1.01%) 1 | 0 / 109 (0.00%) 0 |
| Urinary Tract Infection subjects affected / exposed occurrences (all) | 16 / 231 (6.93%) 27 | 6 / 99 (6.06%) 7 | 1 / 109 (0.92%) 3 |
| Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all) | 42 / 231 (18.18%) 53 | 13 / 99 (13.13%) 13 | 2 / 109 (1.83%) 3 |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 22 / 231 (9.52%) 27 | 3 / 99 (3.03%) 4 | 3 / 109 (2.75%) 3 |

| | | | |
|---|---|--|--|
| Non-serious adverse events | Open-Label Treatment Period: Placebo/Vandetanib 300 mg | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 70 / 79 (88.61%) | | |
| Vascular disorders Hypertension subjects affected / exposed occurrences (all) | 15 / 79 (18.99%) 18 | | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) | 12 / 79 (15.19%) 13 | | |
| Fatigue subjects affected / exposed occurrences (all) | 13 / 79 (16.46%) 16 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 0 / 79 (0.00%) 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|--------------------------------|------------------|--|--|
| Cough | | | |
| subjects affected / exposed | 3 / 79 (3.80%) | | |
| occurrences (all) | 4 | | |
| Dysphonia | | | |
| subjects affected / exposed | 4 / 79 (5.06%) | | |
| occurrences (all) | 4 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 11 / 79 (13.92%) | | |
| occurrences (all) | 11 | | |
| Dyspnoea Exertional | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences (all) | 0 | | |
| Epistaxis | | | |
| subjects affected / exposed | 3 / 79 (3.80%) | | |
| occurrences (all) | 4 | | |
| Haemoptysis | | | |
| subjects affected / exposed | 4 / 79 (5.06%) | | |
| occurrences (all) | 4 | | |
| Oropharyngeal Pain | | | |
| subjects affected / exposed | 3 / 79 (3.80%) | | |
| occurrences (all) | 3 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 2 / 79 (2.53%) | | |
| occurrences (all) | 2 | | |
| Depression | | | |
| subjects affected / exposed | 4 / 79 (5.06%) | | |
| occurrences (all) | 4 | | |
| Insomnia | | | |
| subjects affected / exposed | 6 / 79 (7.59%) | | |
| occurrences (all) | 6 | | |
| Investigations | | | |
| Electrocardiogram Qt Prolonged | | | |
| subjects affected / exposed | 7 / 79 (8.86%) | | |
| occurrences (all) | 8 | | |
| Weight Increased | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 4 | | |
| Weight Decreased subjects affected / exposed occurrences (all) | 5 / 79 (6.33%) 5 | | |
| Nervous system disorders | | | |
| Dizziness subjects affected / exposed occurrences (all) | 7 / 79 (8.86%) 7 | | |
| Dysgeusia subjects affected / exposed occurrences (all) | 3 / 79 (3.80%) 3 | | |
| Headache subjects affected / exposed occurrences (all) | 5 / 79 (6.33%) 5 | | |
| Paraesthesia subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 5 | | |
| Tremor subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 4 | | |
| Ear and labyrinth disorders | | | |
| Vertigo subjects affected / exposed occurrences (all) | 5 / 79 (6.33%) 5 | | |
| Eye disorders | | | |
| Corneal Opacity subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 4 | | |
| Vision Blurred subjects affected / exposed occurrences (all) | 5 / 79 (6.33%) 5 | | |
| Gastrointestinal disorders | | | |
| Abdominal Pain subjects affected / exposed occurrences (all) | 5 / 79 (6.33%) 6 | | |
| Abdominal Pain Upper | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 5 / 79 (6.33%) | | |
| occurrences (all) | 5 | | |
| Constipation | | | |
| subjects affected / exposed | 9 / 79 (11.39%) | | |
| occurrences (all) | 9 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 32 / 79 (40.51%) | | |
| occurrences (all) | 39 | | |
| Dry Mouth | | | |
| subjects affected / exposed | 7 / 79 (8.86%) | | |
| occurrences (all) | 7 | | |
| Toothache | | | |
| subjects affected / exposed | 0 / 79 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 18 / 79 (22.78%) | | |
| occurrences (all) | 24 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 4 / 79 (5.06%) | | |
| occurrences (all) | 4 | | |
| Vomiting | | | |
| subjects affected / exposed | 9 / 79 (11.39%) | | |
| occurrences (all) | 9 | | |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 21 / 79 (26.58%) | | |
| occurrences (all) | 25 | | |
| Alopecia | | | |
| subjects affected / exposed | 4 / 79 (5.06%) | | |
| occurrences (all) | 4 | | |
| Dermatitis Acneiform | | | |
| subjects affected / exposed | 4 / 79 (5.06%) | | |
| occurrences (all) | 6 | | |
| Dry Skin | | | |
| subjects affected / exposed | 11 / 79 (13.92%) | | |
| occurrences (all) | 14 | | |

| | | | |
|---|------------------------|--|--|
| Erythema subjects affected / exposed occurrences (all) | 6 / 79 (7.59%) 8 | | |
| Rash subjects affected / exposed occurrences (all) | 25 / 79 (31.65%) 40 | | |
| Pruritus subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 6 | | |
| Photosensitivity Reaction subjects affected / exposed occurrences (all) | 11 / 79 (13.92%) 14 | | |
| Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all) | 7 / 79 (8.86%) 7 | | |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 4 | | |
| Back Pain subjects affected / exposed occurrences (all) | 3 / 79 (3.80%) 3 | | |
| Bone Pain subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | | |
| Myalgia subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 4 | | |
| Musculoskeletal Pain subjects affected / exposed occurrences (all) | 6 / 79 (7.59%) 6 | | |

| | | | |
|--|------------------------|--|--|
| Musculoskeletal Chest Pain subjects affected / exposed occurrences (all) | 2 / 79 (2.53%) 3 | | |
| Muscle Spasms subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 5 | | |
| Neck Pain subjects affected / exposed occurrences (all) | 1 / 79 (1.27%) 1 | | |
| Pain In Extremity subjects affected / exposed occurrences (all) | 6 / 79 (7.59%) 6 | | |
| Infections and infestations Bronchitis subjects affected / exposed occurrences (all) | 2 / 79 (2.53%) 2 | | |
| Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) | 8 / 79 (10.13%) 13 | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 4 / 79 (5.06%) 6 | | |
| Influenza subjects affected / exposed occurrences (all) | 3 / 79 (3.80%) 4 | | |
| Folliculitis subjects affected / exposed occurrences (all) | 5 / 79 (6.33%) 5 | | |
| Urinary Tract Infection subjects affected / exposed occurrences (all) | 5 / 79 (6.33%) 6 | | |
| Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all) | 17 / 79 (21.52%) 19 | | |
| Hypocalcaemia | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 7 / 79 (8.86%) | | |
| occurrences (all) | 9 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 29 June 2006 | Clarified the procedures and requirements for participants who entered post-progression treatment with vandetanib, the secondary objectives of the study and section 5.1 was updated to be in accord with regulatory guidance. |
| 30 May 2007 | Ophthalmologic examinations were added to the study plan, inclusion and exclusion criteria were updated. |
| 15 May 2008 | The study was redefined as a Phase 3 study, language was updated for consistency with other vandetanib studies in the thyroid cancer program. |
| 18 May 2009 | The objectives for the patient reported outcome (PRO) variables were amended, PRO variables and statistical methods for PRO variables were also revised for consistency with changes to study objectives, participant weight was changed from a secondary to an exploratory objective, the co-primary analysis population of participants with a known rearranged during transfection (proto-oncogene) [RET] mutation was removed from the study, further clarification on determination of RET mutation status was provided. |
| 13 January 2010 | The study plan was updated to provide investigators with the option to unblind participants remaining on blinded, randomised therapy. |
| 06 April 2010 | Exploratory objectives and outcome variables were added, Sections 4.6.15 Histopathology, 4.6.16 CTN and CEA expression in tumor tissue, 4.6.17 Analysis of cell signaling pathways, and 4.6.18 Mutation status of oncogenes were newly created. |
| 06 April 2011 | Incorporated procedures for the management of participants who were still receiving study treatment following final planned data analyses and to update the estimated last subject out date. |
| 03 November 2011 | Provided clarification on unblinding participants once the OS endpoint was met, ZD6474 was approved by the Food and Drug Administration for the treatment of symptomatic or progressive medullary thyroid cancer in participants with unresectable locally advanced or metastatic disease, incorporated procedures for the management of participants who were still receiving study treatment following OS analysis, clarified the recording of adverse events for participants who switched from clinical supplies to marketed vandetanib prior to completing the 60 day follow up assessment, provided additional instruction regarding discontinuing participants from therapy once the OS analysis was completed, provided instruction for survival status contact to be completed within 1 week of the data cut-off for the OS analysis, provided clarification on management of participants who were still receiving blinded therapy at the time of OS analysis and on the timing for OS follow up contact once data-off for the OS analysis had occurred, clarified the process for reporting serious adverse events once the OS endpoint was met and the clinical study database was closed to new data, provided information about updated Appendix E and clarification on the use of drugs that were previously found on the Table 1 or Table 2 in Appendix E, version 3 and were no longer listed in Appendix E, version 4, added an unplanned safety analysis in order to update the vandetanib Risk Management Plan as requested by the European Committee for Medicinal Products for Human Use. |

| | |
|------------------|---|
| 29 February 2016 | The AstraZeneca logo and reference to AstraZeneca within the confidentiality statement were deleted from the title page, throughout all sections of the protocol including header and appendices, AstraZeneca was changed to "Genzyme" or "Sponsor.", the Sanofi-Genzyme study code LPS14811 was added to the AstraZeneca study code D4200C00058, the AstraZeneca study drug code ZD6474 was updated to the generic drug name vandetanib, references to ZACTIMA™ were deleted as the name is obsolete, sections regarding pharmacovigilance were updated to reflect the Genzyme environment, correction of minor typographical errors or inconsistencies were made. |
|------------------|---|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported