



Clinical trial results:

A Biomarker-Directed Phase 2 Trial of SY-1425, a Selective Retinoic Acid Receptor Alpha Agonist, in Adult Patients With Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS)

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2017-000783-14 |
| Trial protocol | FR |
| Global end of trial date | 25 January 2023 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 11 February 2024 |
| First version publication date | 11 February 2024 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | SY-1425-201 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02807558 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Syros Pharmaceuticals, Inc. |
| Sponsor organisation address | 35 CambridgePark Drive, 4th Floor, Cambridge, United States, 02140 |
| Public contact | Jason Haas, Syros Pharmaceuticals Inc., jhaas@syros.com |
| Scientific contact | Emily Fearnow, Syros Pharmaceuticals Inc., efearno@syros.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 | 25 January 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 25 January 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 January 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study is to determine the activity of tamibarotene in participants with relapsed/refractory (R/R) AML (administered as a monotherapy or in combination with azacitidine), R/R higher-risk MDS (HR-MDS)(administered as a monotherapy or in combination with daratumumab), newly diagnosed (ND) treatment naïve AML participants who are unlikely to tolerate standard intensive chemotherapy (administered as a monotherapy or in combination with azacitidine), or lower-risk MDS (LR-MDS) (administered as a monotherapy).

Protection of trial subjects:

This study was conducted according to the protocol, the ethical principles that have their origins in the Declaration of Helsinki, including the current International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Consolidated Guideline E6 (R2), and all applicable national and local laws and regulations.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 20 September 2016 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 2 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | France: 47 |
| Country: Number of subjects enrolled | United States: 108 |
| Worldwide total number of subjects | 155 |
| EEA total number of subjects | 47 |

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) | 20 |
| From 65 to 84 years | 122 |
| 85 years and over | 13 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening assessments were conducted within 30 days of dosing.

Period 1

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

Arms

Are arms mutually exclusive? Yes

Arm title R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy

Arm description:

Participants with R/R non-APL AML or R/R HR-MDS received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 1-28 of a 28-day cycle

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tamibarotene |
| Investigational medicinal product code | |
| Other name | SY-1425 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered as specified in the treatment arm.

Arm title Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy

Arm description:

Newly diagnosed, treatment-naïve participants with non-APL AML who were unlikely to tolerate standard intensive chemotherapy received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 1-28 of a 28-day cycle

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tamibarotene |
| Investigational medicinal product code | |
| Other name | SY-1425 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered as specified in the treatment arm.

Arm title LR-MDS: Tamibarotene Monotherapy

Arm description:

Participants with transfusion-dependent lower-risk myelodysplastic syndrome (LR-MDS) without the del-5q abnormality who were refractory to erythropoietin (EPO) treatment or unlikely to respond to EPO treatment received tamibarotene at 6 mg/m²/day in 2 divided doses from Days 1-28 of a 28-day cycle

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

| | |
|--|--------------|
| Investigational medicinal product name | Tamibarotene |
| Investigational medicinal product code | |
| Other name | SY-1425 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|------------------|---|
| Arm title | Newly Diagnosed Non-APL AML: Tamibarotene and Azacitidine |
|------------------|---|

Arm description:

Newly diagnosed, treatment-naive participants with non-APL AML who were unlikely to tolerate standard intensive chemotherapy received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 8-28 of a 28-day cycle, and azacitidine at 75 mg/m² once daily on Days 1-7 of a 28-day cycle

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Azacitidine |
| Investigational medicinal product code | |
| Other name | Vidaza |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Solution for infusion |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|--|--------------|
| Investigational medicinal product name | Tamibarotene |
| Investigational medicinal product code | |
| Other name | SY-1425 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|------------------|---|
| Arm title | R/R non-APL AML: Tamibarotene and Azacitidine |
|------------------|---|

Arm description:

Participants with R/R non-APL AML received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 8-28 of a 28-day cycle, and azacitidine at 75 mg/m² once daily on Days 1-7 of a 28-day cycle

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Azacitidine |
| Investigational medicinal product code | |
| Other name | Vidaza |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Solution for infusion |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|--|--------------|
| Investigational medicinal product name | Tamibarotene |
| Investigational medicinal product code | |
| Other name | SY-1425 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|------------------|---|
| Arm title | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab |
|------------------|---|

Arm description:

Participants with R/R non-APL AML or R/R HR-MDS received tamibarotene at 6 mg/m²/day in 2 divided doses during a 7-day lead-in and on Days 1-28 of a 28-day cycle. Participants also received daratumumab at 16 mg/kg starting on Cycle 1 Day 1 once weekly for 8 weeks, followed by dosing every 2 weeks for 16 weeks, followed by dosing every 4 weeks

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Daratumumab |
| Investigational medicinal product code | |
| Other name | Darzalex |
| Pharmaceutical forms | Injection/infusion |
| Routes of administration | Solution for infusion |

Dosage and administration details:

Administered as specified in the treatment arm.

| | |
|--|--------------|
| Investigational medicinal product name | Tamibarotene |
| Investigational medicinal product code | |
| Other name | SY-1425 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Administered as specified in the treatment arm.

| Number of subjects in period 1 | R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy | Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy | LR-MDS: Tamibarotene Monotherapy |
|--|--|--|--|
| | | | |
| Started | 29 | 2 | 29 |
| Received at Least 1 Dose of Study Drug | 29 | 2 | 29 |
| Response Evaluable Population | 22 | 2 | 27 |
| Completed per Study Protocol | 29 | 2 | 29 |
| Completed Post-Treatment Follow-Up | 1 | 0 | 0 |
| Evaluable for HI | 16 | 2 | 25 |
| Completed | 1 | 0 | 0 |
| Not completed | 28 | 2 | 29 |
| Consent withdrawn by subject | 4 | - | 4 |
| Non-compliance with Study Drug | - | - | 1 |
| Adverse event, non-fatal | - | - | 9 |
| Death | 23 | 2 | 3 |
| Progressive Disease | - | - | 1 |
| Other than specified | 1 | - | 2 |
| Lack of efficacy | - | - | 9 |

| Number of subjects in period 1 | Newly Diagnosed Non-APL AML: Tamibarotene and Azacitidine | R/R non-APL AML: Tamibarotene and Azacitidine | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab |
|--|--|---|--|
| | | | |
| Started | 51 | 28 | 16 |
| Received at Least 1 Dose of Study Drug | 51 | 28 | 16 |
| Response Evaluable Population | 46 | 21 | 12 |
| Completed per Study Protocol | 51 | 27 | 16 |
| Completed Post-Treatment Follow-Up | 6 | 1 ^[1] | 0 |

| | | | |
|--------------------------------|----|----|----|
| Evaluable for HI | 16 | 17 | 9 |
| Completed | 6 | 2 | 0 |
| Not completed | 45 | 26 | 16 |
| Consent withdrawn by subject | 2 | 1 | - |
| Non-compliance with Study Drug | - | - | - |
| Adverse event, non-fatal | - | - | - |
| Death | 43 | 24 | 15 |
| Progressive Disease | - | - | - |
| Other than specified | - | 1 | 1 |
| Lack of efficacy | - | - | - |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Milestones were added to support data presented.

Baseline characteristics

Reporting groups

| | |
|------------------------------|---|
| Reporting group title | R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy |
| Reporting group description: | Participants with R/R non-APL AML or R/R HR-MDS received tamibarotene at 6 mg/m ² /day in 2 divided doses on Days 1-28 of a 28-day cycle |
| Reporting group title | Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy |
| Reporting group description: | Newly diagnosed, treatment-naive participants with non-APL AML who were unlikely to tolerate standard intensive chemotherapy received tamibarotene at 6 mg/m ² /day in 2 divided doses on Days 1-28 of a 28- day cycle |
| Reporting group title | LR-MDS: Tamibarotene Monotherapy |
| Reporting group description: | Participants with transfusion-dependent lower-risk myelodysplastic syndrome (LR-MDS) without the del-5q abnormality who were refractory to erythropoietin (EPO) treatment or unlikely to respond to EPO treatment received tamibarotene at 6 mg/m ² /day in 2 divided doses from Days 1-28 of a 28-day cycle |
| Reporting group title | Newly Diagnosed Non-APL AML: Tamibarotene and Azacitidine |
| Reporting group description: | Newly diagnosed, treatment-naive participants with non-APL AML who were unlikely to tolerate standard intensive chemotherapy received tamibarotene at 6 mg/m ² /day in 2 divided doses on Days 8-28 of a 28-day cycle, and azacitidine at 75 mg/m ² once daily on Days 1-7 of a 28-day cycle |
| Reporting group title | R/R non-APL AML: Tamibarotene and Azacitidine |
| Reporting group description: | Participants with R/R non-APL AML received tamibarotene at 6 mg/m ² /day in 2 divided doses on Days 8-28 of a 28-day cycle, and azacitidine at 75 mg/m ² once daily on Days 1-7 of a 28-day cycle |
| Reporting group title | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab |
| Reporting group description: | Participants with R/R non-APL AML or R/R HR-MDS received tamibarotene at 6 mg/m ² /day in 2 divided doses during a 7-day lead-in and on Days 1-28 of a 28-day cycle. Participants also received daratumumab at 16 mg/kg starting on Cycle 1 Day 1 once weekly for 8 weeks, followed by dosing every 2 weeks for 16 weeks, followed by dosing every 4 weeks |

| Reporting group values | R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy | Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy | LR-MDS: Tamibarotene Monotherapy |
|------------------------|---|---|----------------------------------|
| Number of subjects | 29 | 2 | 29 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 5 | 0 | 2 |
| From 65-84 years | 21 | 2 | 24 |
| 85 years and over | 3 | 0 | 3 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 70.3 | 74.5 | 76.1 |
| standard deviation | ± 13.27 | ± 3.54 | ± 8.40 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 12 | 0 | 10 |
| Male | 17 | 2 | 19 |

| | | | |
|---|----|---|----|
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 1 | 0 | 0 |
| Black Or African American | 3 | 0 | 3 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| White | 25 | 0 | 22 |
| Other | 0 | 1 | 1 |
| Not Reported | 0 | 1 | 3 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic Or Latino | 3 | 2 | 2 |
| Not Hispanic Or Latino | 25 | 0 | 25 |
| Not Reported | 1 | 0 | 2 |

| Reporting group values | Newly Diagnosed Non-APL AML: Tamibarotene and Azacitidine | R/R non-APL AML: Tamibarotene and Azacitidine | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab |
|---|---|---|---|
| Number of subjects | 51 | 28 | 16 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 3 | 5 | 5 |
| From 65-84 years | 43 | 21 | 11 |
| 85 years and over | 5 | 2 | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 76.0 | 72.0 | 62.9 |
| standard deviation | ± 6.89 | ± 12.19 | ± 13.36 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 19 | 15 | 8 |
| Male | 32 | 13 | 8 |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 2 | 1 | 0 |
| Black Or African American | 2 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| White | 30 | 18 | 14 |
| Other | 2 | 0 | 0 |
| Not Reported | 15 | 9 | 2 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic Or Latino | 6 | 3 | 2 |
| Not Hispanic Or Latino | 29 | 16 | 13 |
| Not Reported | 16 | 9 | 1 |

| Reporting group values | Total | | |
|-------------------------------|-------|--|--|
| Number of subjects | 155 | | |

| | | | |
|---|-----|--|--|
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 20 | | |
| From 65-84 years | 122 | | |
| 85 years and over | 13 | | |
| Age continuous Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 64 | | |
| Male | 91 | | |
| Race Units: Subjects | | | |
| American Indian or Alaska Native | 0 | | |
| Asian | 4 | | |
| Black Or African American | 8 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| White | 109 | | |
| Other | 4 | | |
| Not Reported | 30 | | |
| Ethnicity Units: Subjects | | | |
| Hispanic Or Latino | 18 | | |
| Not Hispanic Or Latino | 108 | | |
| Not Reported | 29 | | |

End points

End points reporting groups

| | |
|-----------------------|---|
| Reporting group title | R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy |
|-----------------------|---|

Reporting group description:

Participants with R/R non-APL AML or R/R HR-MDS received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 1-28 of a 28-day cycle

| | |
|-----------------------|---|
| Reporting group title | Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy |
|-----------------------|---|

Reporting group description:

Newly diagnosed, treatment-naïve participants with non-APL AML who were unlikely to tolerate standard intensive chemotherapy received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 1-28 of a 28-day cycle

| | |
|-----------------------|----------------------------------|
| Reporting group title | LR-MDS: Tamibarotene Monotherapy |
|-----------------------|----------------------------------|

Reporting group description:

Participants with transfusion-dependent lower-risk myelodysplastic syndrome (LR-MDS) without the del-5q abnormality who were refractory to erythropoietin (EPO) treatment or unlikely to respond to EPO treatment received tamibarotene at 6 mg/m²/day in 2 divided doses from Days 1-28 of a 28-day cycle

| | |
|-----------------------|---|
| Reporting group title | Newly Diagnosed Non-APL AML: Tamibarotene and Azacitidine |
|-----------------------|---|

Reporting group description:

Newly diagnosed, treatment-naïve participants with non-APL AML who were unlikely to tolerate standard intensive chemotherapy received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 8-28 of a 28-day cycle, and azacitidine at 75 mg/m² once daily on Days 1-7 of a 28-day cycle

| | |
|-----------------------|---|
| Reporting group title | R/R non-APL AML: Tamibarotene and Azacitidine |
|-----------------------|---|

Reporting group description:

Participants with R/R non-APL AML received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 8-28 of a 28-day cycle, and azacitidine at 75 mg/m² once daily on Days 1-7 of a 28-day cycle

| | |
|-----------------------|---|
| Reporting group title | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab |
|-----------------------|---|

Reporting group description:

Participants with R/R non-APL AML or R/R HR-MDS received tamibarotene at 6 mg/m²/day in 2 divided doses during a 7-day lead-in and on Days 1-28 of a 28-day cycle. Participants also received daratumumab at 16 mg/kg starting on Cycle 1 Day 1 once weekly for 8 weeks, followed by dosing every 2 weeks for 16 weeks, followed by dosing every 4 weeks

| | |
|----------------------------|---|
| Subject analysis set title | ND Non-APL AML: Tamibarotene and Azacitidine: RARA-Positive |
|----------------------------|---|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Participants from the "Newly Diagnosed Non-APL AML: Tamibarotene and Azacitidine" arm who were positive for the RARA super-enhancer associated biomarker (RARA-positive) were included in this sub-group analysis.

Participants who were unlikely to tolerate standard intensive chemotherapy received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 8-28 of a 28-day cycle, and azacitidine at 75 mg/m² once daily on Days 1-7 of a 28-day cycle.

| | |
|----------------------------|---|
| Subject analysis set title | ND Non-APL AML: Tamibarotene and Azacitidine: RARA-Negative |
|----------------------------|---|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Participants from the "Newly Diagnosed Non-APL AML: Tamibarotene and Azacitidine" arm who were negative for the RARA super-enhancer associated biomarker (RARA-negative) were included in this sub-group analysis.

Participants who were unlikely to tolerate standard intensive chemotherapy received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 8-28 of a 28-day cycle, and azacitidine at 75 mg/m² once daily on Days 1-7 of a 28-day cycle.

Primary: Overall Response Rate (ORR) in Biomarker Positive AML or HR-MDS Participants Treated With Tamibarotene Monotherapy or in Combination With Azacitidine

| | |
|-----------------|---|
| End point title | Overall Response Rate (ORR) in Biomarker Positive AML or HR-MDS Participants Treated With Tamibarotene Monotherapy or in Combination With Azacitidine ^{[1][2]} |
|-----------------|---|

End point description:

ORR was defined as: AML: number of participants with complete remission (CR), CR with incomplete blood count recovery (CRi), CR with partial hematologic recovery (CRh), partial remission(PR), or morphologic leukemia-free state (MLFS) determined by the investigator per revised International Working Group (IWG) AML criteria. HR-MDS: the number of participants with CR, PR, marrow CR (mCR), or hematologic improvement (HI) determined by the investigator per revised IWG MDS criteria. Measured in the response evaluable population, which included participants who completed 1 cycle of study treatment, and had a follow-up assessment of disease status, and did not have any major protocol violations, or withdrew from the study before completion of Cycle 1 because of documented disease progression. Overall Number of Participants analyzed (N) signifies those who were evaluable for this Endpoint.

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

End point timeframe:

Up to 48 months

Notes:

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

Justification: Data is presented as specified in the statistical analysis plan.

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

Justification: No statistical analyses were planned for this endpoint.

| End point values | R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy | Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy | R/R non-APL AML: Tamibarotene and Azacitidine | ND Non-APL AML: Tamibarotene and Azacitidine: RARA-Positive |
|-----------------------------|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 22 | 2 | 21 | 18 |
| Units: Participants | 2 | 0 | 4 | 12 |

Statistical analyses

No statistical analyses for this end point

Primary: Transfusion Independence Rate (TIR) in LR-MDS Participants Treated With Tamibarotene Monotherapy

| | |
|-----------------|--|
| End point title | Transfusion Independence Rate (TIR) in LR-MDS Participants Treated With Tamibarotene Monotherapy ^{[3][4]} |
|-----------------|--|

End point description:

TIR was defined as the number of participants who achieved transfusion independence defined as 8 consecutive weeks of red blood cell (RBC) transfusion independence.

Measured in the population evaluable for TIR, which included all participants who received at least 8 weeks of study treatment.

Here, Overall Number of Participants analyzed (N) signifies those who were evaluable for this Endpoint.

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

End point timeframe:

Up to 48 months

Notes:

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

Justification: No statistical analyses were planned for this endpoint.

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

Justification: Data is presented as specified in the statistical analysis plan.

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | LR-MDS: Tamibarotene Monotherapy | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 27 | | | |
| Units: Participants | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Treatment-emergent Adverse Events (TEAEs) Treated With Tamibarotene in Combination With Daratumumab

| | |
|-----------------|---|
| End point title | Number of Participants with Treatment-emergent Adverse Events (TEAEs) Treated With Tamibarotene in Combination With Daratumumab ^{[5][6]} |
|-----------------|---|

End point description:

A TEAE was any untoward medical occurrence associated with use of a study drug/study participation, whether or not considered related to study drug after first dose. A TEAE was any unfavorable/unintended sign (including abnormal laboratory finding), symptom, or disease temporally associated with the study drug. A serious TEAE resulted in death, was life-threatening, required inpatient hospitalization/prolongation of existing hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect in the offspring of a participant who received study drug or other important medical events. Measured in the safety population, which included all screened participants who received any amount of study drug (tamibarotene or combination treatment). A summary of serious and all other non-serious adverse events regardless of causality is located in the Reported Adverse Events module.

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

End point timeframe:

Up to 48 months

Notes:

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

Justification: No statistical analyses were planned for this endpoint.

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

Justification: Data is presented as specified in the statistical analysis plan

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 16 | | | |
| Units: Participants | | | | |
| TEAE | 16 | | | |

| | | | | |
|------------------------|----|--|--|--|
| Treatment-emergent SAE | 12 | | | |
|------------------------|----|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: ORR in AML Participants Positive for the RARA Super-enhancer Associated Biomarker Treated With Tamibarotene Combination With Azacitidine

| | |
|-----------------|---|
| End point title | ORR in AML Participants Positive for the RARA Super-enhancer Associated Biomarker Treated With Tamibarotene Combination With Azacitidine ^[7] |
|-----------------|---|

End point description:

ORR was defined as: AML: the number of participants with CR, CRi, CRh, PR, or MLFS as determined by the investigator per the revised IWG AML criteria.

Measured in the response evaluable population (which included participants who completed 1 cycle of study treatment, and had a follow-up assessment of disease status, and did not have any major protocol violations, or withdrew from the study before completion of Cycle 1 because of documented disease progression) in participants who were RARA-positive. Here, Overall Number of Participants analyzed (N) signifies those who were evaluable for this Endpoint.

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

End point timeframe:

Up to 48 months

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Per prespecified analysis, data were not collected for this Endpoint for the "R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy" arm, the "Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy" arm, and the "R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab" arm as there were fewer than 5 responders per arm. Data are presented per specifications in the statistical analysis plan.

| End point values | R/R non-APL AML: Tamibarotene and Azacitidine | ND Non-APL AML: Tamibarotene and Azacitidine: RARA-Positive | | |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 21 | 18 | | |
| Units: Participants | 4 | 12 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ORR in AML Participants Positive for the Interferon Regulatory Factor 8 (IRF8) Biomarker and Negative for the RARA Super-enhancer Associated Biomarker Treated With Tamibarotene in Combination With Azacitidine

| | |
|-----------------|---|
| End point title | ORR in AML Participants Positive for the Interferon Regulatory Factor 8 (IRF8) Biomarker and Negative for the RARA Super-enhancer Associated Biomarker Treated With Tamibarotene in |
|-----------------|---|

End point description:

ORR was defined as: AML: number of participants with CR, CRi, CRh, PR, or MLFS determined by the investigator per the revised IWG AML criteria.

Measured in the response evaluable population (which included participants who completed 1 cycle of study treatment, had a follow-up assessment of disease status, did not have any major protocol violations, or withdrew from the study before completion of Cycle 1 because of documented disease progression) in participants who were positive for the IRF8 biomarker and negative for the RARA super-enhancer associated biomarker. Here, Overall Number of Participants analyzed (N) signifies those who were evaluable for this Endpoint.

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

End point timeframe:

Up to 48 months

Notes:

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

Justification: Per prespecified analysis, data were collected for this Endpoint only for the arm that enrolled the IRF8-positive participants and that included 5 or more responders. Data are presented per specifications in the statistical analysis plan.

| End point values | Newly Diagnosed Non-APL AML: Tamibarotene and Azacitidine | | | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 4 | | | |
| Units: Participants | 2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ORR in AML Participants Negative for the RARA Super-enhancer Associated Biomarker Treated With Tamibarotene Combination With Azacitidine

| | |
|-----------------|--|
| End point title | ORR in AML Participants Negative for the RARA Super-enhancer Associated Biomarker Treated With Tamibarotene Combination With Azacitidine |
|-----------------|--|

End point description:

ORR was defined as:

AML: the number of participants with CR, CRi, CRh, PR, or MLFS as determined by the investigator per the revised IWG AML criteria.

Measured in the response evaluable population, which included participants who completed 1 cycle of study treatment, and had a follow-up assessment of disease status, and did not have any major protocol violations, or withdrew from the study before completion of Cycle 1 because of documented disease progression. Here, Overall Number of Participants analyzed (N) signifies those who were evaluable for this Endpoint. Per prespecified analysis, data were collected for this Endpoint only for the arm that enrolled the RARA-negative participants and that included 5 or more responders. Data are presented per specifications in the statistical analysis plan.

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

End point timeframe:

Up to 48 months

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | ND Non-APL AML: Tamibarotene and Azacitidine: RARA-Negative | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 28 | | | |
| Units: Participants | 12 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ORR for AML or HR-MDS Participants Treated With Tamibarotene in Combination With Daratumumab

| | |
|-----------------|---|
| End point title | ORR for AML or HR-MDS Participants Treated With Tamibarotene in Combination With Daratumumab ^[9] |
|-----------------|---|

End point description:

ORR was defined as:

AML: the number of participants with CR, CRi, CRh, PR, or MLFS as determined by the investigator per the revised IWG AML criteria.

HR-MDS: the number of participants with CR, PR, mCR, or HI as determined by the investigator per the revised IWG MDS criteria.

Measured in the response evaluable population (which included participants who completed 1 cycle of study treatment, and had a follow-up assessment of disease status, and did not have any major protocol violations, or withdrew from the study before completion of Cycle 1 because of documented disease progression) who had evaluable data for the endpoint.

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

End point timeframe:

Up to 48 months

Notes:

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

Justification: Data is presented as specified in the statistical analysis plan.

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 12 | | | |
| Units: Participants | 2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Event-Free Survival (EFS) in AML and HR-MDS Participants Treated With Tamibarotene in Combination With Azacitidine

| | |
|-----------------|--|
| End point title | Event-Free Survival (EFS) in AML and HR-MDS Participants Treated With Tamibarotene in Combination With Azacitidine ^[10] |
|-----------------|--|

End point description:

EFS was defined as time from first treatment until date of documentation of disease relapse following CR, CRi, or death, whichever occurred first. If the participant did not achieve a CR, EFS was defined as the point of progression or death, whichever occurred first.

Measured in the safety population, which included all screened participants who received any amount of study drug (tamibarotene or combination treatment). Here, Overall Number of Participants analyzed (N) signifies those who were evaluable for this Endpoint.

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

End point timeframe:

Up to 48 months

Notes:

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

Justification: Per prespecified analysis, data were not collected for the Non-APL AML: Tamibarotene Monotherapy arm as there were fewer than 5 participants in the arm. Data are presented per specifications in the statistical analysis plan.

| End point values | R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy | R/R non-APL AML: Tamibarotene and Azacitidine | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab | ND Non-APL AML: Tamibarotene and Azacitidine: RARA-Positive |
|----------------------------------|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 29 | 28 | 16 | 22 |
| Units: months | | | | |
| median (confidence interval 95%) | 2.6 (1.2 to 2.8) | 3.3 (1.9 to 5.5) | 1.2 (1.1 to 2.1) | 8.3 (3.1 to 11.8) |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) in AML Participants Treated With Tamibarotene in Combination With Azacitidine

| | |
|-----------------|--|
| End point title | Duration of Response (DOR) in AML Participants Treated With Tamibarotene in Combination With Azacitidine ^[11] |
|-----------------|--|

End point description:

DOR was defined as time from first date of response CR, CRi, CRh, MLFS or PR until the date of relapse. 99999 = upper confidence interval was not estimable.

Measured in the response evaluable population, which included participants who completed 1 cycle of study treatment, and had a follow-up assessment of disease status, and did not have any major protocol violations, or withdrew from the study before completion of Cycle 1 because of documented disease progression. Here, Overall Number of Participants analyzed (N) signifies those who were evaluable for this Endpoint.

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

End point timeframe:

Up to 48 months

Notes:

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

Justification: Justification: As prespecified, analysis of DOR was not performed for any of the

Tamibarotene Monotherapy arms, or R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab arm, as there were fewer than 5 responders in those study arms. Data is presented as specified in the statistical analysis plan.

| End point values | R/R non-APL AML: Tamibarotene and Azacitidine | ND Non-APL AML: Tamibarotene and Azacitidine: RARA-Positive | | |
|----------------------------------|--|---|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 21 | 18 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 5.9 (1.0 to 99999) | 10.8 (2.9 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in AML and HR-MDS Participants Treated With Tamibarotene Monotherapy, or in Combination With Azacitidine or Daratumumab

| | |
|-----------------|---|
| End point title | Overall Survival (OS) in AML and HR-MDS Participants Treated With Tamibarotene Monotherapy, or in Combination With Azacitidine or Daratumumab ^[12] |
|-----------------|---|

End point description:

OS was defined as the time from first treatment until death from any cause.

Measured in the safety population, which included all screened participants who received any amount of study drug (tamibarotene or combination treatment). Here, Overall Number of Participants analyzed (N) signifies those who were evaluable for this Endpoint.

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

End point timeframe:

Up to 48 months

Notes:

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

Justification: Per planned analysis, data was not collected for LR-MDS: Tamibarotene Monotherapy arm for this Endpoint and analysis of OS was not performed for Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy as there were fewer than 5 participants in this study arm. All-cause mortality is reported in the Reported Adverse Events module. Data is presented as specified in the statistical analysis plan.

| End point values | R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy | R/R non-APL AML: Tamibarotene and Azacitidine | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab | ND Non-APL AML: Tamibarotene and Azacitidine: RARA-Positive |
|----------------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 29 | 28 | 16 | 22 |
| Units: months | | | | |
| median (confidence interval 95%) | 5.7 (2.7 to 7.1) | 5.9 (2.7 to 11.0) | 3.6 (1.8 to 4.6) | 11.7 (6.6 to 15.8) |

Statistical analyses

No statistical analyses for this end point

Secondary: Hematologic Improvement (HI) in AML, HR-MDS and LR-MDS Participants Treated With Tamibarotene Monotherapy, or in Combination With Azacitidine or Daratumumab

| | |
|-----------------|--|
| End point title | Hematologic Improvement (HI) in AML, HR-MDS and LR-MDS Participants Treated With Tamibarotene Monotherapy, or in Combination With Azacitidine or Daratumumab ^[13] |
|-----------------|--|

End point description:

HI was defined according to the modified IWG response criteria for MDS as the number of participants with a response (lasting at least 8 weeks) after first treatment, including erythroid response, platelet response, or neutrophil response.

Measured in the population evaluable for HI, which included all participants who received at least 8 weeks of study treatment.

Here, Overall Number of Participants analyzed (N) signifies those who were evaluable for this Endpoint.

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

End point timeframe:

Up to 48 months

Notes:

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

Justification: Data is presented as specified in the statistical analysis plan.

| End point values | R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy | Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy | LR-MDS: Tamibarotene Monotherapy | R/R non-APL AML: Tamibarotene and Azacitidine |
|-----------------------------|---|---|----------------------------------|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 16 | 2 | 25 | 17 |
| Units: Participants | 3 | 0 | 1 | 1 |

| End point values | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab | ND Non-APL AML: Tamibarotene and Azacitidine: RARA-Positive | | |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 9 | 16 | | |
| Units: Participants | 0 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with TEAEs Number of Participants with Adverse Events in AML and MDS participants treated with tamibarotene monotherapy or in combination with azacitidine

| | |
|-----------------|---|
| End point title | Number of Participants with TEAEs Number of Participants with Adverse Events in AML and MDS participants treated with tamibarotene monotherapy or in combination with azacitidine ^[14] |
|-----------------|---|

End point description:

A TEAE was any untoward medical occurrence associated with use of a study drug/study participation, whether or not considered related to study drug after first dose. A TEAE was any unfavorable/unintended sign (including abnormal laboratory finding), symptom, or disease temporally associated with the study drug. A serious TEAE resulted in death, was life-threatening, required inpatient hospitalization/prolongation of existing hospitalization, persistent or significant disability/incapacity, congenital anomaly/birth defect in the offspring of a participant who received study drug or other important medical events. Measured in the safety population, which included all screened participants who received any amount of study drug (tamibarotene or combination treatment). A summary of serious and all other non-serious adverse events regardless of causality is located in the Reported Adverse Events module.

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

End point timeframe:

Up to 48 months

Notes:

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

Justification: Data is presented as specified in the statistical analysis plan.

| End point values | R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy | Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy | LR-MDS: Tamibarotene Monotherapy | Newly Diagnosed Non-APL AML: Tamibarotene and Azacitidine |
|-----------------------------|---|---|----------------------------------|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 29 | 2 | 29 | 51 |
| Units: Participants | | | | |
| TEAE | 29 | 2 | 29 | 51 |
| Treatment-emergent SAE | 16 | 2 | 15 | 43 |

| End point values | R/R non-APL AML: Tamibarotene and Azacitidine | | | |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 28 | | | |
| Units: Participants | | | | |
| TEAE | 27 | | | |
| Treatment-emergent SAE | 20 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 48 months

Adverse event reporting additional description:

Measured in the safety population, which included all screened participants who received any amount of study drug (tamibarotene or combination treatment).

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 19 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy |
|-----------------------|---|

Reporting group description:

Participants with R/R non-APL AML or R/R HR-MDS received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 1-28 of a 28-day cycle.

| | |
|-----------------------|---|
| Reporting group title | Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy |
|-----------------------|---|

Reporting group description:

Newly diagnosed, treatment-naïve participants with non-APL AML who were unlikely to tolerate standard intensive chemotherapy received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 1-28 of a 28-day cycle.

| | |
|-----------------------|----------------------------------|
| Reporting group title | LR-MDS: Tamibarotene Monotherapy |
|-----------------------|----------------------------------|

Reporting group description:

Participants with transfusion-dependent lower-risk myelodysplastic syndrome (LR-MDS) without the del-5q abnormality who were refractory to erythropoietin (EPO) treatment or unlikely to respond to EPO treatment received tamibarotene at 6 mg/m²/day in 2 divided doses from Days 1-28 of a 28-day cycle

| | |
|-----------------------|---|
| Reporting group title | Newly Diagnosed Non-APL AML: Tamibarotene and Azacitidine |
|-----------------------|---|

Reporting group description:

Newly diagnosed, treatment-naïve participants with non-APL AML who were unlikely to tolerate standard intensive chemotherapy received tamibarotene at 6 mg/m²/day in 2 divided doses on Days 8-28 of a 28-day cycle, and azacitidine at 75 mg/m² once daily on Days 1-7 of a 28-day cycle

This arm included both RARA-positive and RARA-negative participants with newly diagnosed Non-APL AML treated with tamibarotene and azacitidine.

| | |
|-----------------------|---|
| Reporting group title | R/R non-APL AML: Tamibarotene and Azacitidine |
|-----------------------|---|

Reporting group description:

Participants with R/R non-APL AML received tamibarotene from Days 8-28 of a 28-day cycle, and azacitidine on Days 1-7 of a 28-day cycle.

| | |
|-----------------------|---|
| Reporting group title | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab |
|-----------------------|---|

Reporting group description:

Participants with R/R non-APL AML or R/R HR-MDS received tamibarotene during a 7-day lead-in and on Days 1-28 of a 28-day cycle. Participants also received daratumumab on Cycle 1 Day 1 weekly for 8 weeks, followed by dosing every 2 weeks for 16 weeks, followed by dosing every 4 weeks.

| Serious adverse events | R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy | Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy | LR-MDS: Tamibarotene Monotherapy |
|---|---|---|----------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 16 / 29 (55.17%) | 2 / 2 (100.00%) | 15 / 29 (51.72%) |

| | | | |
|---|----------------|---------------|----------------|
| number of deaths (all causes) | 23 | 2 | 3 |
| number of deaths resulting from adverse events | | | |
| Vascular disorders | | | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (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 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vasculitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |

| | | | |
|--|----------------|---------------|----------------|
| Postmenopausal haemorrhage subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| 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 embolism | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary granuloma | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| 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 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |

| | | | |
|---|----------------|---------------|-----------------|
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (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 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| 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 arrest | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina pectoris | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiomyopathy | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cranial nerve disorder | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (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 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydrocephalus | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (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 |
| Neuralgia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 2 (50.00%) | 0 / 29 (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 |
| Syncope | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lacunar stroke | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Partial seizures | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |

| | | | |
|---|-----------------|---------------|----------------|
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 6 / 29 (20.69%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukostasis syndrome | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysphagia | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| 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 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (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 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (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 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenic colitis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (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 | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| 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 allergic | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| 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 and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Renal failure | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal injury | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urethral stenosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| 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 | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone pain | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (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 |
| Muscle haemorrhage | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 2 (50.00%) | 0 / 29 (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 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|-----------------|
| Flank pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Infection | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (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 |
| Lung infection | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (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 |
| Pharyngeal abscess | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 4 / 29 (13.79%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia fungal | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 2 (50.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pneumonia parainfluenzae viral | | | |

| | | | |
|---|----------------|---------------|-----------------|
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (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 |
| Pneumonia staphylococcal | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Septic shock | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (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 |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| 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 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Klebsiella bacteraemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomonas infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary mycosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| 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 infective | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticulitis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterobacter pneumonia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia bacteraemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| 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 abscess | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaria | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nocardiosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Proteus infection | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serratia sepsis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Streptococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 0 / 29 (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 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lactic acidosis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Newly Diagnosed Non-APL AML: Tamibarotene and Azacitidine | R/R non-APL AML: Tamibarotene and Azacitidine | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab |
|--|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 43 / 51 (84.31%) | 20 / 28 (71.43%) | 12 / 16 (75.00%) |
| number of deaths (all causes) | 43 | 24 | 15 |
| number of deaths resulting from adverse events | | | |
| Vascular disorders | | | |
| Orthostatic hypotension | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Vasculitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 | | | |
| Pyrexia | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 1 / 5 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Reproductive system and breast disorders | | | |
| Postmenopausal haemorrhage | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 | | | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Pulmonary granuloma | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 2 / 16 (12.50%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Lung disorder | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Mental status changes | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Overdose | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| 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 myocardial infarction | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Angina unstable | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Cardiomyopathy | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Myocardial infarction | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Nervous system disorders | | | |
| Cranial nerve disorder | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydrocephalus | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| 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 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Headache | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Lacunar stroke | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Partial seizures | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |

| | | | |
|---|------------------|-----------------|-----------------|
| subjects affected / exposed | 12 / 51 (23.53%) | 9 / 28 (32.14%) | 7 / 16 (43.75%) |
| occurrences causally related to treatment / all | 1 / 13 | 1 / 11 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Leukostasis syndrome | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Lymphopenia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| 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 obstruction | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Neutropenic colitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Pancreatitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Renal failure | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 injury | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Urethral stenosis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone pain | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Muscle haemorrhage | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| 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 | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Groin pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Infections and infestations | | | |
| Infection | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| 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 infection | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngeal abscess | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 8 / 51 (15.69%) | 3 / 28 (10.71%) | 3 / 16 (18.75%) |
| occurrences causally related to treatment / all | 1 / 9 | 0 / 3 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia fungal | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pneumonia parainfluenzae viral | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia staphylococcal | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | 4 / 28 (14.29%) | 3 / 16 (18.75%) |
| occurrences causally related to treatment / all | 0 / 5 | 1 / 6 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Klebsiella bacteraemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomonas infection | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| 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 mycosis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Arthritis infective | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Atypical pneumonia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Enterobacter pneumonia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia bacteraemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Lung abscess | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Malaria | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Nocardiosis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Proteus infection | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Pyelonephritis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Serratia sepsis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Skin infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Streptococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Lactic acidosis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Failure to thrive | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 2 / 16 (12.50%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Gout | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (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 |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | R/R Non-APL AML or R/R HR-MDS: Tamibarotene Monotherapy | Newly Diagnosed Non-APL AML: Tamibarotene Monotherapy | LR-MDS: Tamibarotene Monotherapy |
|---|---|---|----------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 29 / 29 (100.00%) | 2 / 2 (100.00%) | 29 / 29 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Fibrous histiocytoma | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Superficial spreading melanoma stage unspecified | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---------------------------------|----------------|-----------------|-----------------|
| Anal cancer | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endometrial cancer | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Pallor | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 2 |
| Vascular insufficiency | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Venous thrombosis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 2 | 0 | 2 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 2 | 0 | 3 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 2 / 2 (100.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Thrombophlebitis superficial | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombosis | | | |

| | | | |
|--|----------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Hot flush subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 2 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Erythema subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Surgical and medical procedures Shoulder arthroplasty subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| General disorders and administration site conditions Adverse drug reaction subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Asthenia subjects affected / exposed occurrences (all) | 4 / 29 (13.79%) 4 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Catheter site erythema subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Catheter site pain subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Chills subjects affected / exposed occurrences (all) | 4 / 29 (13.79%) 4 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Crepitations subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Device related thrombosis subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Exercise tolerance decreased | | | |

| | | | |
|------------------------------|------------------|----------------|-----------------|
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Facial pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 0 | 0 | 2 |
| Fatigue | | | |
| subjects affected / exposed | 12 / 29 (41.38%) | 0 / 2 (0.00%) | 9 / 29 (31.03%) |
| occurrences (all) | 13 | 0 | 9 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 2 (50.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 1 | 1 |
| Injection site bruising | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 1 | 0 | 1 |
| Injection site haemorrhage | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 1 | 0 | 3 |
| Medical device pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Medical device site erythema | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Oedema peripheral | | | |
| subjects affected / exposed | 8 / 29 (27.59%) | 1 / 2 (50.00%) | 5 / 29 (17.24%) |
| occurrences (all) | 12 | 1 | 6 |
| Pain | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 2 | 0 | 2 |
| Pyrexia | | | |
| subjects affected / exposed | 8 / 29 (27.59%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 8 | 0 | 3 |
| Catheter site rash | | | |

| | | | |
|---------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Inflammatory pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site irritation | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site nodule | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site reaction | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |

| | | | |
|--|---------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Peripheral swelling subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Systemic inflammatory response syndrome subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Catheter site swelling subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Early satiety subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Immune system disorders Acute graft versus host disease subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Vulvovaginal pain subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Ovarian vein thrombosis subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Perineal pain subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Postmenopausal haemorrhage subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Vaginal haemorrhage | | | |

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|--|----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Bronchiectasis | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Cough | | | |
| subjects affected / exposed occurrences (all) | 7 / 29 (24.14%) 7 | 1 / 2 (50.00%) 1 | 4 / 29 (13.79%) 4 |
| Dyspnoea | | | |
| subjects affected / exposed occurrences (all) | 8 / 29 (27.59%) 8 | 0 / 2 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Dyspnoea exertional | | | |
| subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Epistaxis | | | |
| subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 3 | 1 / 2 (50.00%) 1 | 2 / 29 (6.90%) 2 |
| Hypopnoea | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Hypoxia | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 3 / 29 (10.34%) 3 |
| Lung disorder | | | |
| subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Nasal congestion | | | |
| subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 3 / 29 (10.34%) 3 |
| Nasal dryness | | | |
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Oropharyngeal pain | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 2 | 0 | 1 |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Rales | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 0 | 0 | 2 |
| Rhonchi | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Sneezing | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 0 | 0 | 2 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Tachypnoea | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tonsillar hypertrophy | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acute promyelocytic leukaemia differentiation syndrome | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---------------------------------------|----------------|---------------|----------------|
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngeal haemorrhage | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary mass | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory acidosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |

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|---|----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal mucosal ulcer | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngospasm | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 0 | 0 | 3 |
| Delirium | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 1 | 0 | 3 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 3 | 0 | 2 |
| Hallucination, Visual acuity reduced | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|---------------------|---------------------|----------------------|
| Mental status changes subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Panic attack subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Psychomotor retardation subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Genito-pelvic pain/penetration disorder subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Hallucination, Olfactory subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Investigations | | | |
| Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 3 / 29 (10.34%) 4 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 4 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Amylase increased subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 1 / 2 (50.00%) 6 | 0 / 29 (0.00%) 0 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 0 / 2 (0.00%) 0 | 2 / 29 (6.90%) 3 |
| Blood cholesterol increased subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 3 / 29 (10.34%) 3 |
| Blood phosphorus decreased | | | |

| | | | |
|---|----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Breath sounds abnormal | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac murmur | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| High density lipoprotein decreased | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 0 | 0 | 3 |
| Lipase decreased | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Lipase increased | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 2 | 0 | 5 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 4 / 29 (13.79%) |
| occurrences (all) | 1 | 0 | 9 |
| Platelet count decreased | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 3 / 29 (10.34%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 6 | 0 | 1 |
| Respiratory rate increased | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin turgor decreased | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Vitamin K decreased | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight decreased | | | |
| subjects affected / exposed | 6 / 29 (20.69%) | 1 / 2 (50.00%) | 6 / 29 (20.69%) |
| occurrences (all) | 12 | 2 | 6 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 1 | 0 | 5 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood uric acid increased | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Coronavirus test positive | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory syncytial virus test positive | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Troponin I increased | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|----------------------|--------------------|----------------------|
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 0 / 2 (0.00%) 0 | 5 / 29 (17.24%) 5 |
| Chest X-ray abnormal subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Heart rate irregular subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Lymphocyte count decreased subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 3 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Excoriation subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Eye injury subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Fall subjects affected / exposed occurrences (all) | 4 / 29 (13.79%) 5 | 0 / 2 (0.00%) 0 | 4 / 29 (13.79%) 6 |
| Joint dislocation subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Laceration subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Post procedural haematoma subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Rib fracture | | | |

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| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Scratch | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Animal bite | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eschar | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Face injury | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural site reaction | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Transfusion reaction | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Transfusion-related circulatory overload | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|---------------------|--------------------|---------------------|
| Infusion related reaction subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Periorbital haemorrhage subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Skin abrasion subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Thermal burn subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Congenital, familial and genetic disorders Macroglossia subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 0 / 2 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Atrial flutter subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 2 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Atrial tachycardia subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Bradycardia subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Nodal rhythm subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Palpitations | | | |

| | | | |
|-------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 3 | 0 | 2 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 2 (50.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Tachycardia | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiomyopathy | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Coronary artery insufficiency | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ventricular hypokinesia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pericarditis | | | |

| | | | |
|--|-----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Cognitive disorder subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Cranial nerve disorder subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Disturbance in attention subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Dizziness subjects affected / exposed occurrences (all) | 9 / 29 (31.03%) 10 | 1 / 2 (50.00%) 3 | 1 / 29 (3.45%) 1 |
| Dizziness postural subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Dysgeusia subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 3 | 0 / 2 (0.00%) 0 | 3 / 29 (10.34%) 3 |
| Encephalopathy subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Facial paresis subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Haemorrhage intracranial subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 5 / 29 (17.24%) 5 | 1 / 2 (50.00%) 1 | 2 / 29 (6.90%) 3 |

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| Memory impairment | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 1 | 0 | 1 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Paraesthesia | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 2 | 0 | 1 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Seizure | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Sinus headache | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Speech disorder | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Syncope | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tongue paralysis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Tremor | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Ageusia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

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| Akathisia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ataxia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Carotid artery thrombosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Coordination abnormal | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nerve compression | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cerebellar syndrome | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperaesthesia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypogeusia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Parkinson's disease | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

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| Parkinsonism | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Partial seizures | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 6 / 29 (20.69%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 12 | 0 | 4 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 6 / 29 (20.69%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 12 | 0 | 4 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 2 | 0 | 2 |
| Splenic lesion | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 1 | 0 | 4 |
| Disseminated intravascular coagulation | | | |

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| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymph node pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytopenic purpura | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thymus disorder | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Ear discomfort | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Excessive cerumen production | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| External ear pain | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypoacusis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 2 | 0 | 1 |

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| Mastoid effusion | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Cerumen impaction | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deafness unilateral | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Conjunctival haemorrhage | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dry eye | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Eye disorder | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye irritation | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Eye pain | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Retinal haemorrhage | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Retinal vascular disorder | | | |

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|--|----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Vision blurred subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 3 | 1 / 2 (50.00%) 1 | 0 / 29 (0.00%) 0 |
| Exophthalmos subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Ocular hyperaemia subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Photophobia subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Blindness subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 1 / 2 (50.00%) 1 | 0 / 29 (0.00%) 0 |
| Abdominal distension subjects affected / exposed occurrences (all) | 5 / 29 (17.24%) 5 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Abdominal pain subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 0 / 2 (0.00%) 0 | 3 / 29 (10.34%) 3 |
| Abdominal rigidity subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 1 / 2 (50.00%) 1 | 0 / 29 (0.00%) 0 |
| Ascites subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Constipation subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 0 / 2 (0.00%) 0 | 4 / 29 (13.79%) 4 |

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| Diarrhoea | | | |
| subjects affected / exposed | 8 / 29 (27.59%) | 0 / 2 (0.00%) | 4 / 29 (13.79%) |
| occurrences (all) | 12 | 0 | 5 |
| Dry mouth | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | 1 / 2 (50.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 3 | 1 | 2 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 1 | 0 | 3 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 0 | 0 | 3 |
| Flatulence | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 2 | 0 | 1 |
| Gingival bleeding | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Lip dry | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Nausea | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | 1 / 2 (50.00%) | 4 / 29 (13.79%) |
| occurrences (all) | 4 | 1 | 4 |

| | | | |
|------------------------------|-----------------|----------------|-----------------|
| Oral pain | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rectal ulcer | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 1 | 0 | 1 |
| Vomiting | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | 1 / 2 (50.00%) | 4 / 29 (13.79%) |
| occurrences (all) | 3 | 1 | 4 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Angina bullosa haemorrhagica | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Faecaloma | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

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| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip swelling | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Melaena | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Noninfective gingivitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral mucosal blistering | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Periodontal disease | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tongue haematoma | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip haemorrhage | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

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| Gingival pain subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Hyperbilirubinaemia subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Hepatic cirrhosis subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 6 / 29 (20.69%) 7 | 1 / 2 (50.00%) 1 | 10 / 29 (34.48%) 14 |
| Blister subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Cold sweat subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Dry skin subjects affected / exposed occurrences (all) | 5 / 29 (17.24%) 5 | 0 / 2 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Hyperhidrosis subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Night sweat subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 3 | 0 / 2 (0.00%) 0 | 2 / 29 (6.90%) 2 |
| Onychomadesis subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Papule | | | |

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| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Petechiae | | | |
| subjects affected / exposed | 6 / 29 (20.69%) | 1 / 2 (50.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 6 | 1 | 2 |
| Pruritus | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | 0 / 2 (0.00%) | 4 / 29 (13.79%) |
| occurrences (all) | 5 | 0 | 4 |
| Purpura | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 1 | 0 | 1 |
| Rash | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 6 | 0 | 1 |
| Rash generalised | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 6 | 0 | 3 |
| Rash pruritic | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin discolouration | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin hyperpigmentation | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin induration | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 1 | 0 | 1 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin mass | | | |

| | | | |
|-----------------------------|----------------|---------------|-----------------|
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin necrosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin ulcer | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 3 | 0 | 4 |
| Eczema | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nodular rash | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Prurigo | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus generalised | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyoderma gangrenosum | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scab | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin erosion | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin exfoliation | | | |

| | | | |
|----------------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stasis dermatitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sticky skin | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chronic papillomatous dermatitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis psoriasiform | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis bullous | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Drug eruption | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 3 | 0 | 2 |
| Chromaturia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysuria | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
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| Micturition urgency | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 1 | 0 | 1 |
| Nocturia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 2 (50.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 0 | 1 | 2 |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary tract pain | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 1 | 0 | 3 |
| Urine odour abnormal | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Chronic kidney disease | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Incontinence | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urethral stenosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary hesitation | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
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| Urinary retention subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Urine flow decreased subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Endocrine disorders | | | |
| Cushingoid subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 5 / 29 (17.24%) 7 | 1 / 2 (50.00%) 1 | 4 / 29 (13.79%) 5 |
| Arthritis subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Back pain subjects affected / exposed occurrences (all) | 4 / 29 (13.79%) 5 | 1 / 2 (50.00%) 3 | 4 / 29 (13.79%) 5 |
| Bone pain subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 1 / 2 (50.00%) 1 | 1 / 29 (3.45%) 2 |
| Bursitis subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 1 / 29 (3.45%) 1 |
| Groin pain subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Intervertebral disc protrusion subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 2 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Joint range of motion decreased | | | |

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| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscular weakness | | | |
| subjects affected / exposed | 5 / 29 (17.24%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 6 | 0 | 3 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 1 / 2 (50.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 2 | 1 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 5 / 29 (17.24%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 5 | 0 | 1 |
| Neck pain | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 7 / 29 (24.14%) | 1 / 2 (50.00%) | 4 / 29 (13.79%) |
| occurrences (all) | 9 | 2 | 4 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Spondylolisthesis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Tendonitis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 2 | 0 | 1 |
| Amyotrophy | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fistula | | | |

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|---------------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flank pain | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intervertebral disc compression | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myositis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Periarthritis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Polymyalgia rheumatica | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tendon disorder | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint instability | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint stiffness | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

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| Bacterial vaginosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Cellulitis | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 4 | 0 | 1 |
| Clostridium bacteriaemia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Furuncle | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Klebsiella bacteriaemia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Klebsiella infection | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Molluscum contagiosum | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Oral candidiasis | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |

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|---|-----------------|---------------|-----------------|
| Otitis externa | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Perineal abscess | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Phlebitis infective | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rash pustular | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 0 | 0 | 2 |
| Skin infection | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 1 | 0 | 3 |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Urinary tract infection | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 1 / 2 (50.00%) 1 | 4 / 29 (13.79%) 4 |
| Abscess oral subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Acute sinusitis subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Bronchitis subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Catheter site infection subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Conjunctivitis subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Corona virus infection subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Cystitis subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Cystitis bacterial subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Device related infection subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Diverticulitis subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Enterococcal bacteraemia subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 2 (0.00%) 0 | 0 / 29 (0.00%) 0 |
| Erysipelas | | | |

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|-------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paronychia | | | |

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|--------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Soft tissue infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinea infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fungal skin infection | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 7 / 29 (24.14%) | 1 / 2 (50.00%) | 8 / 29 (27.59%) |
| occurrences (all) | 8 | 1 | 8 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Fluid overload | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 1 | 0 | 1 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 0 | 0 | 3 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 0 | 0 | 5 |
| Hypernatraemia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 1 | 0 | 1 |

| | | | |
|-----------------------------|------------------|----------------|------------------|
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 11 / 29 (37.93%) | 1 / 2 (50.00%) | 14 / 29 (48.28%) |
| occurrences (all) | 20 | 4 | 30 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 1 | 0 | 2 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 3 | 0 | 2 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 2 (0.00%) | 2 / 29 (6.90%) |
| occurrences (all) | 2 | 0 | 2 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 3 / 29 (10.34%) |
| occurrences (all) | 1 | 0 | 4 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 1 | 0 | 1 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 1 / 29 (3.45%) |
| occurrences (all) | 0 | 0 | 1 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|----------------|---------------|----------------|
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypovolaemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lactic acidosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic alkalosis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 2 (0.00%) | 0 / 29 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Newly Diagnosed Non-APL AML: Tamibarotene and Azacitidine | R/R non-APL AML: Tamibarotene and Azacitidine | R/R non-APL AML or R/R HR-MDS: Tamibarotene and Daratumumab |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 50 / 51 (98.04%) | 27 / 28 (96.43%) | 15 / 16 (93.75%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Fibrous histiocytoma | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Superficial spreading melanoma stage unspecified | | | |

| | | | |
|---|----------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Anal cancer subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Endometrial cancer subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Squamous cell carcinoma of skin subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 16 (0.00%) 0 |
| Vascular disorders | | | |
| Pallor subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Vascular insufficiency subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Venous thrombosis subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Hypertension subjects affected / exposed occurrences (all) | 3 / 51 (5.88%) 6 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 2 |
| Hypotension subjects affected / exposed occurrences (all) | 6 / 51 (11.76%) 7 | 1 / 28 (3.57%) 4 | 1 / 16 (6.25%) 1 |
| Deep vein thrombosis subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Haematoma subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 4 / 28 (14.29%) 4 | 0 / 16 (0.00%) 0 |
| Thrombophlebitis superficial subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |

| | | | |
|--|------------------------|-----------------------|---------------------|
| Thrombosis subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Hot flush subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Erythema subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Surgical and medical procedures Shoulder arthroplasty subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| General disorders and administration site conditions Adverse drug reaction subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Asthenia subjects affected / exposed occurrences (all) | 11 / 51 (21.57%) 15 | 5 / 28 (17.86%) 11 | 0 / 16 (0.00%) 0 |
| Catheter site erythema subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Catheter site pain subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Chills subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 4 / 28 (14.29%) 5 | 0 / 16 (0.00%) 0 |
| Crepitations subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Device related thrombosis subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Exercise tolerance decreased | | | |

| | | | |
|------------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 19 / 51 (37.25%) | 9 / 28 (32.14%) | 4 / 16 (25.00%) |
| occurrences (all) | 34 | 13 | 5 |
| Gait disturbance | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 0 | 1 |
| Injection site bruising | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site haemorrhage | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Medical device pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Medical device site erythema | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 19 / 51 (37.25%) | 4 / 28 (14.29%) | 4 / 16 (25.00%) |
| occurrences (all) | 24 | 7 | 4 |
| Pain | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 3 | 0 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 17 / 51 (33.33%) | 6 / 28 (21.43%) | 1 / 16 (6.25%) |
| occurrences (all) | 32 | 8 | 2 |
| Catheter site rash | | | |

| | | | |
|---------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Impaired healing | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Inflammatory pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injection site erythema | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Injection site irritation | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site nodule | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 3 / 28 (10.71%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Injection site reaction | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Non-cardiac chest pain | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 3 | 2 / 28 (7.14%) 2 | 0 / 16 (0.00%) 0 |
| Peripheral swelling subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 16 (0.00%) 0 |
| Systemic inflammatory response syndrome subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 1 / 28 (3.57%) 2 | 0 / 16 (0.00%) 0 |
| Catheter site swelling subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Early satiety subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Immune system disorders Acute graft versus host disease subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Vulvovaginal pain subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Ovarian vein thrombosis subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Perineal pain subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Postmenopausal haemorrhage subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Vaginal haemorrhage | | | |

| | | | |
|--|------------------------|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Bronchiectasis | | | |
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Cough | | | |
| subjects affected / exposed occurrences (all) | 9 / 51 (17.65%) 10 | 3 / 28 (10.71%) 5 | 3 / 16 (18.75%) 5 |
| Dyspnoea | | | |
| subjects affected / exposed occurrences (all) | 13 / 51 (25.49%) 19 | 6 / 28 (21.43%) 8 | 3 / 16 (18.75%) 4 |
| Dyspnoea exertional | | | |
| subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 2 / 16 (12.50%) 2 |
| Epistaxis | | | |
| subjects affected / exposed occurrences (all) | 5 / 51 (9.80%) 7 | 7 / 28 (25.00%) 9 | 2 / 16 (12.50%) 2 |
| Hypopnoea | | | |
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Hypoxia | | | |
| subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 2 | 2 / 28 (7.14%) 3 | 0 / 16 (0.00%) 0 |
| Lung disorder | | | |
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Nasal congestion | | | |
| subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 3 / 28 (10.71%) 3 | 1 / 16 (6.25%) 2 |
| Nasal dryness | | | |
| subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Oropharyngeal pain | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 4 / 51 (7.84%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences (all) | 4 | 1 | 1 |
| Pleural effusion | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 3 / 28 (10.71%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rales | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 3 / 28 (10.71%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Rhonchi | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sneezing | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 28 (7.14%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 2 | 1 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 2 / 28 (7.14%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachypnoea | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 28 (7.14%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 2 | 1 |
| Tonsillar hypertrophy | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Acute promyelocytic leukaemia differentiation syndrome | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Acute pulmonary oedema | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---------------------------------------|----------------|----------------|----------------|
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dysphonia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Laryngeal haemorrhage | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pulmonary mass | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Respiratory acidosis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinorrhoea | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 51 (5.88%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasal mucosal ulcer | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Laryngospasm | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 6 / 51 (11.76%) | 2 / 28 (7.14%) | 0 / 16 (0.00%) |
| occurrences (all) | 6 | 2 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Delirium | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 3 / 28 (10.71%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Depression | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 0 / 28 (0.00%) | 2 / 16 (12.50%) |
| occurrences (all) | 4 | 0 | 2 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 6 / 51 (11.76%) | 2 / 28 (7.14%) | 2 / 16 (12.50%) |
| occurrences (all) | 8 | 3 | 2 |
| Hallucination, Visual acuity reduced | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Mental status changes subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Panic attack subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Psychomotor retardation subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 2 / 28 (7.14%) 3 | 0 / 16 (0.00%) 0 |
| Genito-pelvic pain/penetration disorder subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Hallucination, Olfactory subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Investigations | | | |
| Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 4 / 51 (7.84%) 8 | 2 / 28 (7.14%) 2 | 1 / 16 (6.25%) 1 |
| Amylase increased subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 3 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 3 | 2 / 28 (7.14%) 2 | 1 / 16 (6.25%) 1 |
| Blood cholesterol increased subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 5 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 4 / 51 (7.84%) 4 | 2 / 28 (7.14%) 3 | 0 / 16 (0.00%) 0 |
| Blood phosphorus decreased | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breath sounds abnormal | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac murmur | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| High density lipoprotein decreased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 2 / 16 (12.50%) |
| occurrences (all) | 0 | 0 | 2 |
| Lipase decreased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 7 | 0 | 2 |
| Platelet count decreased | | | |

| | | | |
|---|------------------|-----------------|----------------|
| subjects affected / exposed | 4 / 51 (7.84%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 9 | 0 | 5 |
| Respiratory rate increased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin turgor decreased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin K decreased | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 18 / 51 (35.29%) | 5 / 28 (17.86%) | 1 / 16 (6.25%) |
| occurrences (all) | 28 | 9 | 2 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 6 | 0 | 1 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 2 / 28 (7.14%) | 0 / 16 (0.00%) |
| occurrences (all) | 4 | 2 | 0 |
| Blood uric acid increased | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Coronavirus test positive | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 0 | 1 |
| Respiratory syncytial virus test positive | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Troponin I increased | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|----------------------|-----------------------|----------------------|
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 3 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Chest X-ray abnormal subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Heart rate irregular subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 2 / 16 (12.50%) 2 |
| Lymphocyte count decreased subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 9 / 51 (17.65%) 9 | 3 / 28 (10.71%) 3 | 1 / 16 (6.25%) 1 |
| Excoriation subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Eye injury subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Fall subjects affected / exposed occurrences (all) | 7 / 51 (13.73%) 8 | 5 / 28 (17.86%) 10 | 1 / 16 (6.25%) 3 |
| Joint dislocation subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Laceration subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Post procedural haematoma subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Rib fracture | | | |

| | | | |
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| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scratch | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Animal bite | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eschar | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Face injury | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Procedural site reaction | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Road traffic accident | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Transfusion reaction | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 2 | 0 | 1 |
| Transfusion-related circulatory overload | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|---------------------|----------------------|----------------------|
| Infusion related reaction subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 5 / 16 (31.25%) 5 |
| Periorbital haemorrhage subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Skin abrasion subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Thermal burn subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Congenital, familial and genetic disorders Macroglossia subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 16 (0.00%) 0 |
| Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 3 / 28 (10.71%) 3 | 0 / 16 (0.00%) 0 |
| Atrial flutter subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Atrial tachycardia subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Bradycardia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 2 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Nodal rhythm subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Palpitations | | | |

| | | | |
|-------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 3 / 51 (5.88%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 28 (7.14%) | 2 / 16 (12.50%) |
| occurrences (all) | 0 | 2 | 2 |
| Tachycardia | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences (all) | 3 | 1 | 1 |
| Angina unstable | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 1 | 1 |
| Cardiomyopathy | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Coronary artery insufficiency | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ventricular hypokinesia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pericarditis | | | |

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|--|------------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Nervous system disorders | | | |
| Cerebrovascular accident subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Cognitive disorder subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Cranial nerve disorder subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Disturbance in attention subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 11 / 51 (21.57%) 15 | 4 / 28 (14.29%) 8 | 0 / 16 (0.00%) 0 |
| Dizziness postural subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Dysgeusia subjects affected / exposed occurrences (all) | 4 / 51 (7.84%) 5 | 3 / 28 (10.71%) 3 | 0 / 16 (0.00%) 0 |
| Encephalopathy subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 16 (0.00%) 0 |
| Facial paresis subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Haemorrhage intracranial subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 6 / 51 (11.76%) 8 | 3 / 28 (10.71%) 4 | 1 / 16 (6.25%) 1 |

| | | | |
|-------------------------------|----------------|----------------|----------------|
| Memory impairment | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 1 | 1 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences (all) | 2 | 1 | 1 |
| Presyncope | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus headache | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Speech disorder | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tongue paralysis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences (all) | 3 | 2 | 1 |
| Ageusia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|----------------------------------|----------------|----------------|----------------|
| Akathisia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ataxia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Balance disorder | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences (all) | 2 | 1 | 1 |
| Carotid artery thrombosis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Coordination abnormal | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Nerve compression | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Cerebellar syndrome | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperaesthesia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypogeusia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 2 / 28 (7.14%) | 0 / 16 (0.00%) |
| occurrences (all) | 3 | 3 | 0 |
| Parkinson's disease | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|------------------|-----------------|-----------------|
| Parkinsonism | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Partial seizures | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 13 / 51 (25.49%) | 5 / 28 (17.86%) | 4 / 16 (25.00%) |
| occurrences (all) | 40 | 12 | 11 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 3 / 28 (10.71%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 9 / 51 (17.65%) | 2 / 28 (7.14%) | 1 / 16 (6.25%) |
| occurrences (all) | 25 | 18 | 1 |
| Splenic lesion | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 12 / 51 (23.53%) | 2 / 28 (7.14%) | 6 / 16 (37.50%) |
| occurrences (all) | 32 | 4 | 30 |
| Disseminated intravascular coagulation | | | |

| | | | |
|--|-----------------------|----------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Leukopenia subjects affected / exposed occurrences (all) | 9 / 51 (17.65%) 18 | 2 / 28 (7.14%) 3 | 4 / 16 (25.00%) 13 |
| Lymph node pain subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 16 (0.00%) 0 |
| Lymphopenia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 2 | 1 / 28 (3.57%) 1 | 0 / 16 (0.00%) 0 |
| Splenomegaly subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Thrombocytopenic purpura subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 1 / 28 (3.57%) 1 | 1 / 16 (6.25%) 1 |
| Thymus disorder subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 16 (0.00%) 0 |
| Ear and labyrinth disorders | | | |
| Ear discomfort subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 2 / 28 (7.14%) 2 | 0 / 16 (0.00%) 0 |
| Ear pain subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 3 / 28 (10.71%) 3 | 1 / 16 (6.25%) 1 |
| Excessive cerumen production subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 16 (0.00%) 0 |
| External ear pain subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Hypoacusis subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Mastoid effusion | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cerumen impaction | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Deafness unilateral | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctival haemorrhage | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dry eye | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye disorder | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye irritation | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retinal haemorrhage | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Retinal vascular disorder | | | |

| | | | |
|--|------------------------|------------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Vision blurred subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Exophthalmos subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Ocular hyperaemia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 1 / 28 (3.57%) 1 | 0 / 16 (0.00%) 0 |
| Photophobia subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Blindness subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Abdominal distension subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 2 / 28 (7.14%) 2 | 2 / 16 (12.50%) 2 |
| Abdominal pain subjects affected / exposed occurrences (all) | 6 / 51 (11.76%) 7 | 3 / 28 (10.71%) 4 | 3 / 16 (18.75%) 3 |
| Abdominal rigidity subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Ascites subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Constipation subjects affected / exposed occurrences (all) | 24 / 51 (47.06%) 30 | 10 / 28 (35.71%) 15 | 2 / 16 (12.50%) 2 |

| | | | |
|----------------------------------|------------------|------------------|-----------------|
| Diarrhoea | | | |
| subjects affected / exposed | 17 / 51 (33.33%) | 11 / 28 (39.29%) | 3 / 16 (18.75%) |
| occurrences (all) | 25 | 15 | 3 |
| Dry mouth | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | 3 / 28 (10.71%) | 0 / 16 (0.00%) |
| occurrences (all) | 5 | 3 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 2 / 28 (7.14%) | 0 / 16 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip dry | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Mouth ulceration | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Nausea | | | |
| subjects affected / exposed | 24 / 51 (47.06%) | 14 / 28 (50.00%) | 5 / 16 (31.25%) |
| occurrences (all) | 25 | 18 | 5 |

| | | | |
|------------------------------|------------------|-----------------|-----------------|
| Oral pain | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 1 | 1 |
| Rectal ulcer | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 4 / 28 (14.29%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 6 | 1 |
| Toothache | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 3 / 28 (10.71%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 11 / 51 (21.57%) | 9 / 28 (32.14%) | 6 / 16 (37.50%) |
| occurrences (all) | 13 | 17 | 7 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 0 | 1 |
| Anal fissure | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Angina bullosa haemorrhagica | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 2 / 28 (7.14%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Faecaloma | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lip swelling | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Melaena | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 1 | 1 |
| Noninfective gingivitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oral mucosal blistering | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 1 | 1 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Periodontal disease | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Proctalgia | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Tongue haematoma | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lip haemorrhage | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|------------------------|----------------------|----------------------|
| Gingival pain subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 2 / 28 (7.14%) 2 | 0 / 16 (0.00%) 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Hyperbilirubinaemia subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 3 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Hepatic cirrhosis subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 8 / 51 (15.69%) 12 | 2 / 28 (7.14%) 4 | 1 / 16 (6.25%) 1 |
| Blister subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 1 / 28 (3.57%) 1 | 0 / 16 (0.00%) 0 |
| Cold sweat subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Dry skin subjects affected / exposed occurrences (all) | 10 / 51 (19.61%) 14 | 5 / 28 (17.86%) 5 | 3 / 16 (18.75%) 3 |
| Hyperhidrosis subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Night sweat subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 2 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Onychomadesis subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Papule | | | |

| | | | |
|-----------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Petechiae | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 5 / 28 (17.86%) | 1 / 16 (6.25%) |
| occurrences (all) | 3 | 5 | 1 |
| Pruritus | | | |
| subjects affected / exposed | 12 / 51 (23.53%) | 5 / 28 (17.86%) | 0 / 16 (0.00%) |
| occurrences (all) | 16 | 5 | 0 |
| Purpura | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 3 / 28 (10.71%) | 1 / 16 (6.25%) |
| occurrences (all) | 3 | 3 | 1 |
| Rash | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | 1 / 28 (3.57%) | 3 / 16 (18.75%) |
| occurrences (all) | 6 | 1 | 3 |
| Rash generalised | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | 2 / 28 (7.14%) | 0 / 16 (0.00%) |
| occurrences (all) | 10 | 4 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Skin discolouration | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin hyperpigmentation | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Skin induration | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin mass | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Skin necrosis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Eczema | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nodular rash | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Prurigo | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pruritus generalised | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyoderma gangrenosum | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Scab | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin erosion | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin exfoliation | | | |

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| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stasis dermatitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sticky skin | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Chronic papillomatous dermatitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis psoriasiform | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis bullous | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Drug eruption | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 3 / 28 (10.71%) | 0 / 16 (0.00%) |
| occurrences (all) | 4 | 5 | 0 |
| Chromaturia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysuria | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|-----------------------------|----------------|-----------------|----------------|
| Micturition urgency | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Nocturia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 3 / 28 (10.71%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 3 | 1 |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary tract pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urine odour abnormal | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chronic kidney disease | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Incontinence | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urethral stenosis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary hesitation | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 2 / 28 (7.14%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |

| | | | |
|--|------------------------|-----------------------|----------------------|
| Urinary retention subjects affected / exposed occurrences (all) | 4 / 51 (7.84%) 4 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Urine flow decreased subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Endocrine disorders | | | |
| Cushingoid subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 13 / 51 (25.49%) 15 | 7 / 28 (25.00%) 11 | 3 / 16 (18.75%) 4 |
| Arthritis subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 9 / 51 (17.65%) 11 | 1 / 28 (3.57%) 1 | 2 / 16 (12.50%) 2 |
| Bone pain subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Bursitis subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Groin pain subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Intervertebral disc protrusion subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Joint range of motion decreased | | | |

| | | | |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 1 | 1 |
| Muscular weakness | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 2 / 28 (7.14%) | 1 / 16 (6.25%) |
| occurrences (all) | 5 | 4 | 2 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 0 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 9 / 51 (17.65%) | 3 / 28 (10.71%) | 0 / 16 (0.00%) |
| occurrences (all) | 11 | 3 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 5 / 51 (9.80%) | 4 / 28 (14.29%) | 3 / 16 (18.75%) |
| occurrences (all) | 6 | 7 | 3 |
| Neck pain | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 2 / 28 (7.14%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 7 / 51 (13.73%) | 3 / 28 (10.71%) | 2 / 16 (12.50%) |
| occurrences (all) | 11 | 3 | 2 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spondylolisthesis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tendonitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Amyotrophy | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Fistula | | | |

| | | | |
|---------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Flank pain | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Intervertebral disc compression | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myositis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Periarthritis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Polymyalgia rheumatica | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tendon disorder | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Joint instability | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint stiffness | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|----------------|-----------------|----------------|
| Bacterial vaginosis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Clostridium bacteraemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Furuncle | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes simplex | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Klebsiella bacteraemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Klebsiella infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Molluscum contagiosum | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 4 / 51 (7.84%) | 3 / 28 (10.71%) | 0 / 16 (0.00%) |
| occurrences (all) | 4 | 4 | 0 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|----------------|-----------------|-----------------|
| Otitis externa | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Perineal abscess | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Phlebitis infective | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 3 / 28 (10.71%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Rash pustular | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 2 / 16 (12.50%) |
| occurrences (all) | 2 | 0 | 2 |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 3 / 51 (5.88%) | 2 / 28 (7.14%) | 1 / 16 (6.25%) |
| occurrences (all) | 3 | 4 | 1 |
| Abscess oral | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Acute sinusitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Catheter site infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Corona virus infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cystitis bacterial | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Device related infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Enterococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Erysipelas | | | |

| | | | |
|-------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lung infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oesophageal candidiasis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Oral fungal infection | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Parainfluenzae virus infection | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Paronychia | | | |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Soft tissue infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Tinea infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fungal skin infection | | | |

| | | | |
|--|------------------------|-----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Influenza | | | |
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Lip infection | | | |
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Oral herpes | | | |
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 2 / 16 (12.50%) 3 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed occurrences (all) | 24 / 51 (47.06%) 35 | 9 / 28 (32.14%) 10 | 3 / 16 (18.75%) 4 |
| Dehydration | | | |
| subjects affected / exposed occurrences (all) | 4 / 51 (7.84%) 4 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Fluid overload | | | |
| subjects affected / exposed occurrences (all) | 1 / 51 (1.96%) 1 | 1 / 28 (3.57%) 1 | 0 / 16 (0.00%) 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed occurrences (all) | 4 / 51 (7.84%) 5 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed occurrences (all) | 5 / 51 (9.80%) 6 | 0 / 28 (0.00%) 0 | 1 / 16 (6.25%) 1 |
| Hypernatraemia | | | |
| subjects affected / exposed occurrences (all) | 0 / 51 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |
| Hyperphosphataemia | | | |
| subjects affected / exposed occurrences (all) | 2 / 51 (3.92%) 2 | 0 / 28 (0.00%) 0 | 0 / 16 (0.00%) 0 |

| | | | |
|-----------------------------|------------------|-----------------|-----------------|
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 21 / 51 (41.18%) | 8 / 28 (28.57%) | 5 / 16 (31.25%) |
| occurrences (all) | 68 | 17 | 6 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 7 | 2 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 13 / 51 (25.49%) | 0 / 28 (0.00%) | 3 / 16 (18.75%) |
| occurrences (all) | 15 | 0 | 3 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 2 / 16 (12.50%) |
| occurrences (all) | 0 | 0 | 2 |
| Hyponatraemia | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 0 | 1 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Failure to thrive | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 2 / 28 (7.14%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Gout | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 3 / 51 (5.88%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypovolaemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lactic acidosis | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Malnutrition | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Metabolic alkalosis | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 1 / 28 (3.57%) | 0 / 16 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 2 / 51 (3.92%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 0 / 51 (0.00%) | 0 / 28 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 51 (1.96%) | 0 / 28 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 23 August 2016 | <ul style="list-style-type: none">- The study design was changed to include 2 additional participant populations:<ul style="list-style-type: none">- Newly diagnosed, treatment naïve older participants with non-APL AML who were unlikely to respond to or tolerate standard therapies- Participants with transfusion-dependent LR-MDS without the del 5q abnormality who were refractory to EPO treatment or unlikely to respond to EPO treatment- The study design was changed from a 1-arm study with 2 cohorts stratified by biomarker status into a 4-arm study.- The number of participants to be enrolled was increased to approximately 80 response-evaluable participants enrolling into 4 arms of approximately 20 participants each- Study objectives and endpoints, eligibility criteria, study schema, Schedule of Events, and statistics were updated to align with the revised study design.- The study was updated to exclude use of strong inducers of Cytochrome P450 3A4 (CYP3A4) within 2 weeks prior to first study treatment and throughout the study |
| 20 March 2017 | <ul style="list-style-type: none">- The study design was changed to include an additional arm (Arm 2B) for newly diagnosed, treatment-naïve participants with non-APL AML ≥60 years of age. Participants enrolled in Arm 2B were to receive tamibarotene in combination with azacitidine.- The total number of participants to be enrolled in the study was increased to approximately 100 response-evaluable participants enrolling into 4 arms of approximately 25 participants each.- Participants enrolled in Arms 1, 2A, 2B, and 3 had to be positive for the RARA super-enhancer associated biomarker or IRF8 biomarker.- Newly diagnosed participants with AML enrolled in Arm 2A who achieved a CR, CRi or PR while on tamibarotene monotherapy and then relapsed, or who failed to achieve a CR, CRi or PR after completing at least 4 cycles, were eligible to receive tamibarotene in combination with azacitidine.- Study objectives and endpoints, study schema, statistics, and Schedule of Events were updated to align with the revised study design.- Participants were allowed to enroll in study sites located in both the US and Europe. |
| 07 July 2017 | <ul style="list-style-type: none">- The eligibility criteria for newly diagnosed participants with AML (Arms 2A and 2B) were revised for consistency with the unfit participant population as described in the Ferrara, et al paper (Ferrara 2013).- Clarification was added that assignment to Arm 2A (single-agent tamibarotene) or Arm 2B (tamibarotene/azacitidine) is determined by investigator choice of treatment. |
| 25 April 2018 | <ul style="list-style-type: none">- The sample size in Arm 2B was increased from 25 to 50 participants (approximately 25 biomarker positive and 25 biomarker negative).- Clarification was added that the first primary objective/endpoint will be analyzed in biomarker-positive participants.- A secondary objective/endpoint was added to explore the ORR in Arm 2B.- Inclusion criteria were updated to allow participants in Arm 2B to be enrolled regardless of biomarker result.- The statistical section was updated to include calculation to support new secondary endpoint. |

| | |
|----------------|--|
| 29 March 2019 | <ul style="list-style-type: none"> - The protocol was updated to characterize the clinical activity of the tamibarotene and azacitidine combination in biomarker-positive participants with R/R AML. - Update was made to reflect the additional requirements for daratumumab due to a newly identified risk of hepatitis B reactivation as communicated via administrative letter dated 26 December 2018. - Bone marrow sample collection was updated for participants with AML and HR-MDS to enable the assessment of the extent of a CR. - Central laboratory sampling was updated to allow for adequate sampling and accommodating/reducing a participant's time at each visit. - The Schedule of Events for Arm 4 was updated to add an Hepatitis B virus (HBV) serology test for specific participants. |
| 31 August 2022 | <ul style="list-style-type: none"> - The primary reason for this amendment was to provide a means for the last participant on study treatment (Arm 5) to continue to have access to tamibarotene as long as the participant continues to experience clinical benefit and to discontinue survival follow-up collection for all participants still active on study in post-treatment follow-up (all in Arm 2B). - Protocol was revised to describe the study procedure changes resulting from Amendment 7 for Arm 5 and Arm 2B participants who were still participating in the study at the time of the amendment. - Protocol was revised to update the site requirements and instructions for providing tamibarotene accountability records to the sponsor. - The protocol was revised to update the concomitant medication instructions for CYP3A4 inhibitors and inducers, in alignment with recent updates made to the investigator brochure (IB). - The protocol was revised to differentiate between male and female contraceptive requirements in alignment with recent updates made to the IB. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported