



Clinical trial results: STOPAH: STeroids Or Pentoxifylline for Alcoholic Hepatitis Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2009-013897-42 |
| Trial protocol | GB |
| Global end of trial date | 25 April 2014 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 07 February 2022 |
| First version publication date | 07 February 2022 |

Trial information

Trial identification

| | |
|-----------------------|------------|
| Sponsor protocol code | RHMMED0883 |
|-----------------------|------------|

Additional study identifiers

| | |
|------------------------------------|--|
| ISRCTN number | ISRCTN88782125 |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | MHRA CTA reference number: 11709/0227/001-0001 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | University Hospital Southampton NHS Foundation Trust |
| Sponsor organisation address | Southampton General Hospital, Level E, Laboratory & Pathology Block, SCBR, MP 138, Southampton, United Kingdom, SO16 6YD |
| Public contact | University of Southampton Clinical Trials Unit, University of Southampton Clinical Trials Unit, 0044 2381205154, ctu@soton.ac.uk |
| Scientific contact | University of Southampton Clinical Trials Unit, University of Southampton Clinical Trials Unit, 0044 2381205154, ctu@soton.ac.uk |

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 | 12 September 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 25 April 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 25 April 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To determine whether prednisolone or pentoxifylline improve the 28 day mortality (death rate) from severe alcoholic hepatitis.

Link to the protocol:

https://www.nejm.org/doi/suppl/10.1056/NEJMoa1412278/suppl_file/nejmoa1412278_protocol.pdf

Protection of trial subjects:

See protocol - Link to the protocol:

https://www.nejm.org/doi/suppl/10.1056/NEJMoa1412278/suppl_file/nejmoa1412278_protocol.pdf

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------------|
| Actual start date of recruitment | 20 January 2011 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Scientific research |
| Long term follow-up duration | 1 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|----------------------|
| Country: Number of subjects enrolled | United Kingdom: 1092 |
| Worldwide total number of subjects | 1092 |
| EEA total number of subjects | 1092 |

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) | 1019 |
| From 65 to 84 years | 73 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from January 2011 through February 2014 at 66 hospitals across the United Kingdom. In total, 66 trial sites were opened but subsequently, one site was closed after failing to recruit any patients.

Pre-assignment

Screening details:

A total of 5234 patients were screened for the trial, and after applying inclusion and exclusion criteria, 1103 were randomised and evenly allocated to the four treatment arms. 1092 patients started the trial.

Period 1

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

Arms

| | |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo/Placebo |

Arm description:

All patients were given one capsule containing placebo four times per day. The medication were administered for 28 days

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

Dosage and administration details:

All patients were given one capsule placebo four times per day. The medication were administered for 28 days

| | |
|------------------|--------------|
| Arm title | Placebo/Pred |
|------------------|--------------|

Arm description:

All patients were given one capsule placebo three times per day, plus one capsule containing 40 mg of prednisolone once daily. Both medications were administered for 28 days

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

Dosage and administration details:

Placebo one capsule three times daily for 28 days

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

Dosage and administration details:

Prednisolone was given 40 mg daily for 28 days

| | |
|------------------|-------------|
| Arm title | PTX/Placebo |
|------------------|-------------|

Arm description:

All patients were given one capsule containing 400 mg of PTX three times per day, plus one capsule placebo once daily. Both medications were administered for 28 days

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

Dosage and administration details:

All patients were given one capsule placebo once per day. The medication was administered for 28 days

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

Dosage and administration details:

All patients were given one capsule containing 400 mg of PTX three times per day, administered for 28 days

| | |
|------------------|----------|
| Arm title | PTX/Pred |
|------------------|----------|

Arm description:

All patients were given one capsule containing 400 mg of PTX three times per day, plus one capsule containing 40 mg of prednisolone once daily. Both medications were administered for 28 days.

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

Dosage and administration details:

Prednisolone was given 40 mg daily for 28 days

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

Dosage and administration details:

Pentoxifylline one capsule (400mg) tds for 28 days

| Number of subjects in period 1 | Placebo/Placebo | Placebo/Pred | PTX/Placebo |
|---------------------------------------|-----------------|--------------|-------------|
| Started | 272 | 274 | 273 |
| Completed | 192 | 190 | 184 |
| Not completed | 80 | 84 | 89 |
| Consent withdrawn by subject | 8 | 8 | 12 |
| Early cessation of follow-up | 48 | - | - |
| Early cessation of follow-up | - | 44 | 56 |
| Lost to follow-up | 24 | 32 | 21 |
| Died before randomisation | - | - | - |

| Number of subjects in period 1 | PTX/Pred |
|---------------------------------------|----------|
| Started | 273 |
| Completed | 181 |
| Not completed | 92 |
| Consent withdrawn by subject | 12 |
| Early cessation of follow-up | - |
| Early cessation of follow-up | 44 |
| Lost to follow-up | 35 |
| Died before randomisation | 1 |

Baseline characteristics

Reporting groups

| | |
|---|-----------------|
| Reporting group title | Placebo/Placebo |
| Reporting group description: All patients were given one capsule containing placebo four times per day. The medication were administered for 28 days | |
| Reporting group title | Placebo/Pred |
| Reporting group description: All patients were given one capsule placebo three times per day, plus one capsule containing 40 mg of prednisolone once daily. Both medications were administered for 28 days | |
| Reporting group title | PTX/Placebo |
| Reporting group description: All patients were given one capsule containing 400 mg of PTX three times per day, plus one capsule placebo once daily. Both medications were administered for 28 days | |
| Reporting group title | PTX/Pred |
| Reporting group description: All patients were given one capsule containing 400 mg of PTX three times per day, plus one capsule containing 40 mg of prednisolone once daily. Both medications were administered for 28 days. | |

| Reporting group values | Placebo/Placebo | Placebo/Pred | PTX/Placebo |
|---------------------------------------|-----------------|--------------|-------------|
| Number of subjects | 272 | 274 | 273 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 253 | 254 | 259 |
| Adults 65-84 years | 19 | 20 | 14 |
| Age continuous Units: years | | | |
| arithmetic mean | 48.8 | 49.3 | 47.9 |
| standard deviation | ± 10.3 | ± 10.6 | ± 10.2 |
| Gender categorical Units: Subjects | | | |
| Female | 110 | 97 | 109 |
| Male | 162 | 177 | 164 |

| Reporting group values | PTX/Pred | Total | |
|---------------------------------------|----------|-------|--|
| Number of subjects | 273 | 1092 | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 253 | 1019 | |
| Adults 65-84 years | 20 | 73 | |
| Age continuous Units: years | | | |
| arithmetic mean | 48.6 | - | |
| standard deviation | ± 9.8 | | |
| Gender categorical Units: Subjects | | | |
| Female | 91 | 407 | |
| Male | 182 | 685 | |

End points

End points reporting groups

| | |
|---|---------------------------|
| Reporting group title | Placebo/Placebo |
| Reporting group description: All patients were given one capsule containing placebo four times per day. The medication were administered for 28 days | |
| Reporting group title | Placebo/Pred |
| Reporting group description: All patients were given one capsule placebo three times per day, plus one capsule containing 40 mg of prednisolone once daily. Both medications were administered for 28 days | |
| Reporting group title | PTX/Placebo |
| Reporting group description: All patients were given one capsule containing 400 mg of PTX three times per day, plus one capsule placebo once daily. Both medications were administered for 28 days | |
| Reporting group title | PTX/Pred |
| Reporting group description: All patients were given one capsule containing 400 mg of PTX three times per day, plus one capsule containing 40 mg of prednisolone once daily. Both medications were administered for 28 days. | |
| Subject analysis set title | Prednisolone at day 28 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: mortality among patients who received prednisolone those in the pentoxifylline–placebo group or those in the prednisolone–pentoxifylline group at day 28 | |
| Subject analysis set title | No Prednisolone at day 28 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: mortality among patients who didn` t receive prednisolone at 28 days | |
| Subject analysis set title | No Prednisolone at day 90 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: mortality among patients who didn` t receive prednisolone at 90 days | |
| Subject analysis set title | No Prednisolone at year 1 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: mortality among patients who didn` t receive prednisolone at 1 year | |
| Subject analysis set title | Prednisolone at day 90 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: mortality among patients who received prednisolone those in the pentoxifylline–placebo group or those in the prednisolone–pentoxifylline group at day 90 | |
| Subject analysis set title | Prednisolone at year 1 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: mortality among patients who received prednisolone those in the pentoxifylline–placebo group or those in the prednisolone–pentoxifylline group at year 1 | |
| Subject analysis set title | Pentoxifylline at day 28 |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: mortality among patients who received pentoxifylline those in the pentoxifylline–placebo group or those in the prednisolone–pentoxifylline group at day 28 | |
| Subject analysis set title | Pentoxifylline at day 90 |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

mortality among patients who received pentoxifylline those in the pentoxifylline–placebo group or those in the prednisolone–pentoxifylline group at year 90

| | |
|----------------------------|--------------------------|
| Subject analysis set title | Pentoxifylline at year 1 |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

mortality among patients who received pentoxifylline those in the pentoxifylline–placebo group or those in the prednisolone–pentoxifylline group at year 1

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | No Pentoxifylline at day 28 |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

mortality among patients who didn't received pentoxifylline at day 28

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | No Pentoxifylline at day 90 |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

mortality among patients who didn't receive pentoxifylline at day 90

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | No Pentoxifylline at year 1 |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

mortality among patients who didn't receive pentoxifylline at year 1

Primary: Mortality at day 28

| | |
|-----------------|---------------------|
| End point title | Mortality at day 28 |
|-----------------|---------------------|

End point description:

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

End point timeframe:

28 days

| End point values | Placebo/Placebo | Placebo/Pred | PTX/Placebo | PTX/Pred |
|------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 269 | 266 | 258 | 260 |
| Units: participants who died | 45 | 38 | 50 | 35 |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Treatment interaction between prednisolone-pent |
|----------------------------|---|

Statistical analysis description:

Treatment interaction between prednisolone-pentoxifylline group

| | |
|-------------------|---------------------------------------|
| Comparison groups | PTX/Placebo v Placebo/Pred v PTX/Pred |
|-------------------|---------------------------------------|

| | |
|---|----------------------|
| Number of subjects included in analysis | 784 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.41 |
| Method | Regression, Logistic |

Primary: Mortality Prednisolone at day 28

| | |
|------------------------|----------------------------------|
| End point title | Mortality Prednisolone at day 28 |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| 28 days | |

| End point values | Prednisolone at day 28 | No Prednisolone at day 28 | | |
|---|------------------------|---------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 526 | 527 | | |
| Units: number of participants dies or liver tra | 73 | 95 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Prednisolone at days 28 |
| Comparison groups | Prednisolone at day 28 v No Prednisolone at day 28 |
| Number of subjects included in analysis | 1053 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.06 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.72 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.52 |
| upper limit | 1.01 |

Primary: Mortality Pentoxifylline at day 28

| | |
|-----------------|------------------------------------|
| End point title | Mortality Pentoxifylline at day 28 |
|-----------------|------------------------------------|

End point description:

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

End point timeframe:

28 days

| End point values | Pentoxifylline at day 28 | No Pentoxifylline at day 28 | | |
|---|--------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 518 | 535 | | |
| Units: number of participants dies or liver tra | 85 | 83 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Pentoxifylline at days 28 |
| Comparison groups | Pentoxifylline at day 28 v No Pentoxifylline at day 28 |
| Number of subjects included in analysis | 1053 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.69 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.07 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.77 |
| upper limit | 1.49 |

Secondary: Mortality or liver transplant at day 90 Prednisolone

| | |
|-----------------|--|
| End point title | Mortality or liver transplant at day 90 Prednisolone |
|-----------------|--|

End point description:

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

End point timeframe:

90 days

| End point values | No Prednisolone at day 90 | Prednisolone at day 90 | | |
|--|---------------------------------|---------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 484 | 484 | | |
| Units: number of participants dies or liver tra | 141 | 144 | | |

Statistical analyses

| Statistical analysis title | Prednisolone at days 90 |
|---|--|
| Comparison groups | No Prednisolone at day 90 v Prednisolone at day 90 |
| Number of subjects included in analysis | 968 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.87 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.77 |
| upper limit | 1.35 |

Secondary: Mortality or liver transplant at year 1 Prednisolone

| | |
|------------------------|--|
| End point title | Mortality or liver transplant at year 1 Prednisolone |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 1 year | |

| End point values | No Prednisolone at year 1 | Prednisolone at year 1 | | |
|--|---------------------------------|---------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 376 | 371 | | |
| Units: number of participants dies or liver tra | 211 | 210 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Prednisolone at year 1 |
| Comparison groups | No Prednisolone at year 1 v Prednisolone at year 1 |
| Number of subjects included in analysis | 747 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.94 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.76 |
| upper limit | 1.35 |

Secondary: Mortality or liver transplant at day 90 Pentoxifylline

| | |
|------------------------|--|
| End point title | Mortality or liver transplant at day 90 Pentoxifylline |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 90 days | |

| End point values | Pentoxifylline at day 90 | No Pentoxifylline at day 90 | | |
|---|--------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 478 | 490 | | |
| Units: number of participants dies or liver tra | 139 | 146 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Pentoxifylline at days 90 |
| Comparison groups | Pentoxifylline at day 90 v No Pentoxifylline at day 90 |
| Number of subjects included in analysis | 968 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.81 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.97 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.73 |
| upper limit | 1.28 |

Secondary: Mortality or liver transplant at year 1 Pentoxifylline

| | |
|------------------------|--|
| End point title | Mortality or liver transplant at year 1 Pentoxifylline |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 1 year | |

| End point values | Pentoxifylline at year 1 | No Pentoxifylline at year 1 | | |
|---|--------------------------|-----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 365 | 382 | | |
| Units: number of participants dies or liver tra | 205 | 216 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Pentoxifylline at year 1 |
| Comparison groups | Pentoxifylline at year 1 v No Pentoxifylline at year 1 |
| Number of subjects included in analysis | 747 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.97 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.74 |
| upper limit | 1.33 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

1 year

Adverse event reporting additional description:

AE additional description

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------|
| Reporting group title | Placebo/Placebo |
|-----------------------|-----------------|

Reporting group description: -

| | |
|-----------------------|---------------|
| Reporting group title | Placebo/Pred. |
|-----------------------|---------------|

Reporting group description: -

| | |
|-----------------------|-------------|
| Reporting group title | PTX/Placebo |
|-----------------------|-------------|

Reporting group description: -

| | |
|-----------------------|-----------|
| Reporting group title | PTX/Pred. |
|-----------------------|-----------|

Reporting group description: -

| Serious adverse events | Placebo/Placebo | Placebo/Pred. | PTX/Placebo |
|--|--|--------------------|--------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 106 / 273 (38.83%) | 128 / 273 (46.89%) | 111 / 272 (40.81%) |
| number of deaths (all causes) | 44 | 53 | 43 |
| number of deaths resulting from adverse events | 44 | 53 | 43 |
| Vascular disorders | | | |
| Thromboembolic event | Additional description: Thromboembolic event | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hematoma | Additional description: Hematoma | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 1 / 273 (0.37%) | 2 / 272 (0.74%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Edema limbs | Additional description: Edema limbs | | |

| | | | |
|--|--|-----------------|-----------------|
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multi-organ failure | Additional description: Multi-organ failure | | |
| subjects affected / exposed | 6 / 273 (2.20%) | 3 / 273 (1.10%) | 6 / 272 (2.21%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 4 | 0 / 3 | 0 / 3 |
| General disorders and administration site conditions: Other, specify | Additional description: General disorders and administration site conditions: Other, specify | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | Additional description: Non-cardiac chest pain | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Malaise | Additional description: Malaise | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 2 / 273 (0.73%) | 0 / 272 (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 |
| Social circumstances | | | |
| Social circumstances: Other, specify | Additional description: Social circumstances: Other, specify | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory, thoracic and mediastinal disorders: Other, specify | Additional description: Respiratory, thoracic and mediastinal disorders: Other, specify | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Adult respiratory distress syndrome | Additional description: Adult respiratory distress syndrome | | |

| | | | |
|---|---|-----------------|-----------------|
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 4 / 272 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| Aspiration | Additional description: Aspiration | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (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 |
| Dyspnea | Additional description: Dyspnea | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 4 / 273 (1.47%) | 2 / 272 (0.74%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 4 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Pleural effusion | Additional description: Pleural effusion | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Bronchospasm | Additional description: Bronchospasm | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (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 |
| Hypoxia | Additional description: Hypoxia | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| 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 edema | Additional description: Pulmonary edema | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Epistaxis | Additional description: Epistaxis | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (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 failure | Additional description: Respiratory failure | | |

| | | | |
|---|---|-----------------|-----------------|
| subjects affected / exposed | 1 / 273 (0.37%) | 5 / 273 (1.83%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 0 |
| Psychiatric disorders | Additional description: Psychosis | | |
| Psychosis | | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | Additional description: Suicide attempt | | |
| Suicide attempt | | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (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 |
| Confusion | Additional description: Confusion | | |
| Confusion | | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Psychiatric disorders: Other, specify | Additional description: Psychiatric disorders: Other, specify | | |
| Psychiatric disorders: Other, specify | | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Hallucinations | Additional description: Hallucinations | | |
| Hallucinations | | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 0 / 273 (0.00%) | 0 / 272 (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 |
| Investigations | Additional description: Blood bilirubin increased | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations: Other, specify | Additional description: Investigations: Other, specify | | |
| Investigations: Other, specify | | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 2 / 273 (0.73%) | 0 / 272 (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 |
| Injury, poisoning and procedural | | | |

| | | | |
|--|--|-----------------|-----------------|
| complications Injury, poisoning and procedural complications: Other, specify subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Injury, poisoning and procedural complications: Other, specify | | |
| | 0 / 273 (0.00%) | 2 / 273 (0.73%) | 1 / 272 (0.37%) |
| | 0 / 0 | 0 / 4 | 0 / 1 |
| | 0 / 0 | 0 / 1 | 0 / 0 |
| Hip fracture subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Hip fracture | | |
| | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| | 0 / 1 | 0 / 0 | 0 / 0 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Fall | | |
| | 2 / 273 (0.73%) | 1 / 273 (0.37%) | 2 / 272 (0.74%) |
| | 0 / 2 | 0 / 1 | 0 / 2 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Arterial injury subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Arterial injury | | |
| | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| | 0 / 1 | 0 / 0 | 0 / 0 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Seroma subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Seroma | | |
| | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Fracture subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Fracture | | |
| | 1 / 273 (0.37%) | 2 / 273 (0.73%) | 0 / 272 (0.00%) |
| | 0 / 1 | 0 / 2 | 0 / 0 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Atrial fibrillation | | |
| | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Myocardial infarction | | |
| | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| | 0 / 0 | 0 / 1 | 0 / 0 |
| | 0 / 0 | 0 / 1 | 0 / 0 |

| | | | |
|---|--|-----------------|-----------------|
| Cardiac arrest | Additional description: Cardiac arrest | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 1 / 273 (0.37%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Ventricular tachycardia | Additional description: Ventricular tachycardia | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (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 |
| Chest pain - cardiac | Additional description: Chest pain - cardiac | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Nervous system disorders | | | |
| Stroke | Additional description: Stroke | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 0 / 273 (0.00%) | 0 / 272 (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 |
| Depressed level of consciousness | Additional description: Depressed level of consciousness | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (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 |
| Encephalopathy | Additional description: Encephalopathy | | |
| subjects affected / exposed | 8 / 273 (2.93%) | 4 / 273 (1.47%) | 4 / 272 (1.47%) |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 4 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 2 |
| Intracranial hemorrhage | Additional description: Intracranial hemorrhage | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| 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 | Additional description: Syncope | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 3 / 273 (1.10%) | 0 / 272 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders: Other, | Additional description: Nervous system disorders: Other, specify | | |

| | | | |
|---|--|-----------------|------------------|
| specify | | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Seizure | Additional description: Seizure | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 3 / 273 (1.10%) | 2 / 272 (0.74%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Leukocytosis | Additional description: Leukocytosis | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Anemia | Additional description: Anemia | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 2 / 272 (0.74%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemolysis | Additional description: Hemolysis | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Gastrointestinal disorders | | | |
| Nausea | Additional description: Nausea | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (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 |
| Ascites | Additional description: Ascites | | |
| subjects affected / exposed | 6 / 273 (2.20%) | 8 / 273 (2.93%) | 11 / 272 (4.04%) |
| occurrences causally related to treatment / all | 0 / 7 | 1 / 13 | 0 / 14 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders: Other, specify | Additional description: Gastrointestinal disorders: Other, specify | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 3 / 272 (1.10%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|-----------------|-----------------|
| Colonic perforation subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Colonic perforation | | |
| | 0 / 273 (0.00%) | 2 / 273 (0.73%) | 0 / 272 (0.00%) |
| | 0 / 0 | 2 / 2 | 0 / 0 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Gastrointestinal pain | | |
| | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| | 0 / 0 | 0 / 0 | 0 / 1 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Pancreatitis | | |
| | 1 / 273 (0.37%) | 1 / 273 (0.37%) | 2 / 272 (0.74%) |
| | 1 / 1 | 0 / 1 | 2 / 2 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Abdominal pain | | |
| | 4 / 273 (1.47%) | 5 / 273 (1.83%) | 4 / 272 (1.47%) |
| | 0 / 6 | 1 / 5 | 0 / 4 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Ileus | | |
| | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| | 0 / 0 | 0 / 0 | 0 / 1 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Esophageal hemorrhage subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Esophageal hemorrhage | | |
| | 1 / 273 (0.37%) | 2 / 273 (0.73%) | 0 / 272 (0.00%) |
| | 0 / 1 | 0 / 2 | 0 / 0 |
| | 0 / 1 | 0 / 1 | 0 / 0 |
| Vomiting subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Vomiting | | |
| | 1 / 273 (0.37%) | 1 / 273 (0.37%) | 3 / 272 (1.10%) |
| | 1 / 1 | 0 / 1 | 2 / 3 |
| | 0 / 0 | 0 / 0 | 0 / 0 |
| Esophageal varices hemorrhage subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | Additional description: Esophageal varices hemorrhage | | |
| | 5 / 273 (1.83%) | 5 / 273 (1.83%) | 7 / 272 (2.57%) |
| | 0 / 7 | 1 / 5 | 0 / 7 |
| | 0 / 1 | 0 / 1 | 0 / 4 |
| Duodenal perforation | Additional description: Duodenal perforation | | |
| | | | |

| | | | |
|---|---|------------------|-----------------|
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Enterocolitis | Additional description: Enterocolitis | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal hemorrhage | Additional description: Upper gastrointestinal hemorrhage | | |
| subjects affected / exposed | 5 / 273 (1.83%) | 12 / 273 (4.40%) | 9 / 272 (3.31%) |
| occurrences causally related to treatment / all | 0 / 5 | 2 / 12 | 1 / 10 |
| deaths causally related to treatment / all | 0 / 3 | 1 / 6 | 0 / 4 |
| Abdominal distension | Additional description: Abdominal distension | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 3 / 273 (1.10%) | 3 / 272 (1.10%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | Additional description: Colitis | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal hemorrhage | Additional description: Rectal hemorrhage | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Lower gastrointestinal hemorrhage | Additional description: Lower gastrointestinal hemorrhage | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Colonic obstruction | Additional description: Colonic obstruction | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric hemorrhage | Additional description: Gastric hemorrhage | | |

| | | | |
|---|---|------------------|------------------|
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Constipation | Additional description: Constipation | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhea | Additional description: Diarrhea | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 4 / 272 (1.47%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 4 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatobiliary disorders: Other, specify | Additional description: Hepatobiliary disorders: Other, specify | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic failure | Additional description: Hepatic failure | | |
| subjects affected / exposed | 26 / 273 (9.52%) | 27 / 273 (9.89%) | 23 / 272 (8.46%) |
| occurrences causally related to treatment / all | 0 / 26 | 0 / 27 | 1 / 23 |
| deaths causally related to treatment / all | 0 / 22 | 0 / 14 | 1 / 17 |
| Skin and subcutaneous tissue disorders | | | |
| Skin ulceration | Additional description: Skin ulceration | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxic epidermal necrolysis | Additional description: Toxic epidermal necrolysis | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| 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 | | | |
| Renal and urinary disorders: Other, specify | Additional description: Renal and urinary disorders: Other, specify | | |

| | | | |
|---|--|-----------------|-----------------|
| subjects affected / exposed | 1 / 273 (0.37%) | 5 / 273 (1.83%) | 9 / 272 (3.31%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 5 | 0 / 9 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 4 | 0 / 6 |
| Acute kidney injury | Additional description: Acute kidney injury | | |
| subjects affected / exposed | 9 / 273 (3.30%) | 5 / 273 (1.83%) | 4 / 272 (1.47%) |
| occurrences causally related to treatment / all | 0 / 9 | 1 / 5 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 3 | 0 / 3 | 0 / 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | Additional description: Back pain | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Muscle weakness lower limb | Additional description: Muscle weakness lower limb | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myositis | Additional description: Myositis | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Hepatic infection | Additional description: Hepatic infection | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 2 / 273 (0.73%) | 0 / 272 (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 |
| Endocarditis infective | Additional description: Endocarditis infective | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (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 infection | Additional description: Abdominal infection | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| 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 | Additional description: Sepsis | | |
| subjects affected / exposed | 7 / 273 (2.56%) | 11 / 273 (4.03%) | 6 / 272 (2.21%) |
| occurrences causally related to treatment / all | 1 / 8 | 3 / 11 | 2 / 6 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 4 | 0 / 4 |
| Joint infection | Additional description: Joint infection | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| 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 | Additional description: Skin infection | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 1 / 273 (0.37%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations: Other, specify | Additional description: Infections and infestations: Other, specify | | |
| subjects affected / exposed | 5 / 273 (1.83%) | 8 / 273 (2.93%) | 3 / 272 (1.10%) |
| occurrences causally related to treatment / all | 2 / 6 | 4 / 9 | 1 / 3 |
| deaths causally related to treatment / all | 1 / 3 | 2 / 3 | 0 / 1 |
| Urinary tract infection | Additional description: Urinary tract infection | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | Additional description: Lung infection | | |
| subjects affected / exposed | 11 / 273 (4.03%) | 19 / 273 (6.96%) | 6 / 272 (2.21%) |
| occurrences causally related to treatment / all | 3 / 11 | 12 / 20 | 3 / 6 |
| deaths causally related to treatment / all | 2 / 3 | 5 / 9 | 0 / 1 |
| Metabolism and nutrition disorders | | | |
| Hypoglycemia | Additional description: Hypoglycemia | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (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 |
| Hyperglycemia | Additional description: Hyperglycemia | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 3 / 273 (1.10%) | 0 / 272 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-------------------------------------|-----------------|-----------------|
| Dehydration | Additional description: Dehydration | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|--|--|--|--|
| Serious adverse events | PTX/Pred. | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 116 / 274 (42.34%) | | |
| number of deaths (all causes) | 37 | | |
| number of deaths resulting from adverse events | 37 | | |
| Vascular disorders | | | |
| Thromboembolic event | Additional description: Thromboembolic event | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hematoma | Additional description: Hematoma | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Edema limbs | Additional description: Edema limbs | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Multi-organ failure | Additional description: Multi-organ failure | | |
| subjects affected / exposed | 7 / 274 (2.55%) | | |
| occurrences causally related to treatment / all | 0 / 7 | | |
| deaths causally related to treatment / all | 0 / 7 | | |
| General disorders and administration site conditions: Other, specify | Additional description: General disorders and administration site conditions: Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Non-cardiac chest pain | Additional description: Non-cardiac chest pain | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malaise | Additional description: Malaise | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Social circumstances | | | |
| Social circumstances: Other, specify | Additional description: Social circumstances: Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory, thoracic and mediastinal disorders: Other, specify | Additional description: Respiratory, thoracic and mediastinal disorders: Other, specify | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Adult respiratory distress syndrome | Additional description: Adult respiratory distress syndrome | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Aspiration | Additional description: Aspiration | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnea | Additional description: Dyspnea | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pleural effusion | Additional description: Pleural effusion | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|-----------------|--|
| Bronchospasm | Additional description: Bronchospasm | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Hypoxia | Additional description: Hypoxia | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Pulmonary edema | Additional description: Pulmonary edema | | |
| | subjects affected / exposed | 2 / 274 (0.73%) | |
| | occurrences causally related to treatment / all | 0 / 2 | |
| | deaths causally related to treatment / all | 0 / 2 | |
| Epistaxis | Additional description: Epistaxis | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Respiratory failure | Additional description: Respiratory failure | | |
| | subjects affected / exposed | 5 / 274 (1.82%) | |
| | occurrences causally related to treatment / all | 1 / 5 | |
| | deaths causally related to treatment / all | 1 / 2 | |
| Psychiatric disorders | | | |
| Psychosis | Additional description: Psychosis | | |
| | subjects affected / exposed | 1 / 274 (0.36%) | |
| | occurrences causally related to treatment / all | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Suicide attempt | Additional description: Suicide attempt | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Confusion | Additional description: Confusion | | |
| | subjects affected / exposed | 3 / 274 (1.09%) | |
| | occurrences causally related to treatment / all | 1 / 3 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Psychiatric disorders: Other, specify | | | |
| Additional description: Psychiatric disorders: Other, specify | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hallucinations | Additional description: Hallucinations | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Blood bilirubin increased | Additional description: Blood bilirubin increased | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations: Other, specify | Additional description: Investigations: Other, specify | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Injury, poisoning and procedural complications: Other, specify | Additional description: Injury, poisoning and procedural complications: Other, specify | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hip fracture | Additional description: Hip fracture | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fall | Additional description: Fall | | |
| subjects affected / exposed | 3 / 274 (1.09%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arterial injury | Additional description: Arterial injury | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--------------------------|---|-----------------|--|
| Seroma | Additional description: Seroma | | |
| | subjects affected / exposed | 1 / 274 (0.36%) | |
| | occurrences causally related to treatment / all | 1 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Fracture | Additional description: Fracture | | |
| | subjects affected / exposed | 1 / 274 (0.36%) | |
| | occurrences causally related to treatment / all | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Cardiac disorders | | | |
| | Additional description: Atrial fibrillation | | |
| | subjects affected / exposed | 1 / 274 (0.36%) | |
| | occurrences causally related to treatment / all | 0 / 1 | |
| Myocardial infarction | Additional description: Myocardial infarction | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Cardiac arrest | Additional description: Cardiac arrest | | |
| | subjects affected / exposed | 2 / 274 (0.73%) | |
| | occurrences causally related to treatment / all | 0 / 2 | |
| | deaths causally related to treatment / all | 0 / 2 | |
| Ventricular tachycardia | Additional description: Ventricular tachycardia | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Chest pain - cardiac | Additional description: Chest pain - cardiac | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Nervous system disorders | | | |
| | Additional description: Stroke | | |
| | subjects affected / exposed | 1 / 274 (0.36%) | |
| | occurrences causally related to treatment / all | 0 / 1 | |
| | | | |
| | deaths causally related to treatment / all | 0 / 0 | |
| | | | |
| | | | |

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|---|--|--|--|
| Depressed level of consciousness subjects affected / exposed | Additional description: Depressed level of consciousness | | |
| occurrences causally related to treatment / all | 0 / 274 (0.00%) | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Encephalopathy subjects affected / exposed | Additional description: Encephalopathy | | |
| occurrences causally related to treatment / all | 4 / 274 (1.46%) | | |
| deaths causally related to treatment / all | 0 / 4 | | |
| Intracranial hemorrhage subjects affected / exposed | Additional description: Intracranial hemorrhage | | |
| occurrences causally related to treatment / all | 1 / 274 (0.36%) | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Syncope subjects affected / exposed | Additional description: Syncope | | |
| occurrences causally related to treatment / all | 1 / 274 (0.36%) | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Nervous system disorders: Other, specify | Additional description: Nervous system disorders: Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Seizure subjects affected / exposed | Additional description: Seizure | | |
| occurrences causally related to treatment / all | 2 / 274 (0.73%) | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Blood and lymphatic system disorders Leukocytosis | Additional description: Leukocytosis | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anemia subjects affected / exposed | Additional description: Anemia | | |
| occurrences causally related to treatment / all | 0 / 274 (0.00%) | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|--|--|------------------|--|
| Hemolysis | Additional description: Hemolysis | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Nausea | Additional description: Nausea | | |
| | subjects affected / exposed | 1 / 274 (0.36%) | |
| | occurrences causally related to treatment / all | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Ascites | Additional description: Ascites | | |
| | subjects affected / exposed | 13 / 274 (4.74%) | |
| | occurrences causally related to treatment / all | 0 / 13 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Gastrointestinal disorders: Other, specify | Additional description: Gastrointestinal disorders: Other, specify | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Colonic perforation | Additional description: Colonic perforation | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Gastrointestinal pain | Additional description: Gastrointestinal pain | | |
| | subjects affected / exposed | 1 / 274 (0.36%) | |
| | occurrences causally related to treatment / all | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Pancreatitis | Additional description: Pancreatitis | | |
| | subjects affected / exposed | 3 / 274 (1.09%) | |
| | occurrences causally related to treatment / all | 2 / 3 | |
| | deaths causally related to treatment / all | 1 / 1 | |
| Abdominal pain | Additional description: Abdominal pain | | |
| | subjects affected / exposed | 1 / 274 (0.36%) | |
| | occurrences causally related to treatment / all | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | |

| | | | |
|-----------------------------------|---|------------------|--|
| Ileus | Additional description: Ileus | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Esophageal hemorrhage | Additional description: Esophageal hemorrhage | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Vomiting | Additional description: Vomiting | | |
| | subjects affected / exposed | 2 / 274 (0.73%) | |
| | occurrences causally related to treatment / all | 1 / 2 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Esophageal varices hemorrhage | Additional description: Esophageal varices hemorrhage | | |
| | subjects affected / exposed | 5 / 274 (1.82%) | |
| | occurrences causally related to treatment / all | 0 / 5 | |
| | deaths causally related to treatment / all | 0 / 1 | |
| Duodenal perforation | Additional description: Duodenal perforation | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Enterocolitis | Additional description: Enterocolitis | | |
| | subjects affected / exposed | 1 / 274 (0.36%) | |
| | occurrences causally related to treatment / all | 1 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Upper gastrointestinal hemorrhage | Additional description: Upper gastrointestinal hemorrhage | | |
| | subjects affected / exposed | 13 / 274 (4.74%) | |
| | occurrences causally related to treatment / all | 3 / 18 | |
| | deaths causally related to treatment / all | 0 / 1 | |
| Abdominal distension | Additional description: Abdominal distension | | |
| | subjects affected / exposed | 0 / 274 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | |
| Colitis | Additional description: Colitis | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rectal hemorrhage | Additional description: Rectal hemorrhage | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower gastrointestinal hemorrhage | Additional description: Lower gastrointestinal hemorrhage | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colonic obstruction | Additional description: Colonic obstruction | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Gastric hemorrhage | Additional description: Gastric hemorrhage | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Constipation | Additional description: Constipation | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhea | Additional description: Diarrhea | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Hepatobiliary disorders: Other, specify | Additional description: Hepatobiliary disorders: Other, specify | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic failure | Additional description: Hepatic failure | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 21 / 274 (7.66%) | | |
| occurrences causally related to treatment / all | 1 / 22 | | |
| deaths causally related to treatment / all | 0 / 12 | | |
| Skin and subcutaneous tissue disorders | | | |
| Skin ulceration | Additional description: Skin ulceration | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Toxic epidermal necrolysis | | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Renal and urinary disorders: Other, specify | Additional description: Renal and urinary disorders: Other, specify | | |
| subjects affected / exposed | 3 / 274 (1.09%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 5 / 274 (1.82%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | Additional description: Back pain | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Muscle weakness lower limb | | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myositis | | | |
| | Additional description: Myositis | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Hepatic infection | Additional description: Hepatic infection | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Endocarditis infective | | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal infection | | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 3 / 274 (1.09%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Joint infection | | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin infection | | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations: Other, specify | | | |
| subjects affected / exposed | 3 / 274 (1.09%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| | Additional description: Urinary tract infection | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung infection | Additional description: Lung infection | | |
| subjects affected / exposed | 18 / 274 (6.57%) | | |
| occurrences causally related to treatment / all | 4 / 18 | | |
| deaths causally related to treatment / all | 1 / 7 | | |
| Metabolism and nutrition disorders | | | |
| Hypoglycemia | Additional description: Hypoglycemia | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperglycemia | Additional description: Hyperglycemia | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dehydration | Additional description: Dehydration | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Placebo/Placebo | Placebo/Pred. | PTX/Placebo |
|--|--|-------------------|--------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 106 / 273 (38.83%) | 96 / 273 (35.16%) | 102 / 272 (37.50%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Neoplasms benign, malignant and unspecified (inc cysts and polyps): Other, specify | Additional description: Neoplasms benign, malignant and unspecified (inc cysts and polyps): Other, specify | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify | Additional description: Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify | | |

| | | | |
|---|---|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 2 / 273 (0.73%) 2 | 3 / 273 (1.10%) 3 | 1 / 272 (0.37%) 1 |
| Vascular disorders | Additional description: Peripheral ischemia | | |
| Peripheral ischemia subjects affected / exposed occurrences (all) | 2 / 273 (0.73%) 2 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Vascular disorders : Other, specify | Additional description: Vascular disorders : Other, specify | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Hematoma | Additional description: Hematoma | | |
| subjects affected / exposed occurrences (all) | 1 / 273 (0.37%) 1 | 3 / 273 (1.10%) 3 | 1 / 272 (0.37%) 1 |
| Hypotension | Additional description: Hypotension | | |
| subjects affected / exposed occurrences (all) | 4 / 273 (1.47%) 4 | 1 / 273 (0.37%) 1 | 3 / 272 (1.10%) 3 |
| Thromboembolic event | Additional description: Thromboembolic event | | |
| subjects affected / exposed occurrences (all) | 1 / 273 (0.37%) 1 | 1 / 273 (0.37%) 1 | 1 / 272 (0.37%) 1 |
| General disorders and administration site conditions | Additional description: Fever | | |
| Fever subjects affected / exposed occurrences (all) | 5 / 273 (1.83%) 6 | 6 / 273 (2.20%) 6 | 6 / 272 (2.21%) 6 |
| General disorders and administration site conditions: Other, specify | Additional description: General disorders and administration site conditions: Other, specify | | |
| subjects affected / exposed occurrences (all) | 1 / 273 (0.37%) 1 | 0 / 273 (0.00%) 0 | 2 / 272 (0.74%) 2 |
| Fatigue | Additional description: Fatigue | | |
| subjects affected / exposed occurrences (all) | 3 / 273 (1.10%) 3 | 1 / 273 (0.37%) 1 | 4 / 272 (1.47%) 4 |
| Localised edema | Additional description: Localised edema | | |
| subjects affected / exposed occurrences (all) | 11 / 273 (4.03%) 15 | 5 / 273 (1.83%) 6 | 3 / 272 (1.10%) 3 |
| Hypothermia | Additional description: Hypothermia | | |
| subjects affected / exposed occurrences (all) | 2 / 273 (0.73%) 2 | 1 / 273 (0.37%) 1 | 0 / 272 (0.00%) 0 |
| Injection site reaction | Additional description: Injection site reaction | | |

| | | | |
|--|--|-----------------|-----------------|
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Edema limbs | Additional description: Edema limbs | | |
| subjects affected / exposed | 5 / 273 (1.83%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Infusion related reaction | Additional description: Infusion related reaction | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin infection | Additional description: Skin infection | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Malaise | Additional description: Malaise | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 2 / 273 (0.73%) | 6 / 272 (2.21%) |
| occurrences (all) | 1 | 2 | 6 |
| Facial pain | Additional description: Facial pain | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pruritus | Additional description: Pruritus | | |
| subjects affected / exposed | 4 / 273 (1.47%) | 3 / 273 (1.10%) | 5 / 272 (1.84%) |
| occurrences (all) | 4 | 3 | 5 |
| Non-cardiac chest pain | Additional description: Non-cardiac chest pain | | |
| subjects affected / exposed | 3 / 273 (1.10%) | 2 / 273 (0.73%) | 5 / 272 (1.84%) |
| occurrences (all) | 3 | 2 | 5 |
| Reproductive system and breast disorders | | | |
| Vaginal hemorrhage | Additional description: Vaginal hemorrhage | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erectile dysfunction | Additional description: Erectile dysfunction | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Gynecomastia | Additional description: Gynecomastia | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Reproductive system and breast disorders: Other, specify | Additional description: Reproductive system and breast disorders: Other, specify | | |

| | | | |
|---|---|-----------------|-----------------|
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reporoductive system and breast disorders : Other, specify | Additional description: Reporoductive system and breast disorders : Other, specify | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | Additional description: Pleural effusion | | |
| subjects affected / exposed | 6 / 273 (2.20%) | 2 / 273 (0.73%) | 1 / 272 (0.37%) |
| occurrences (all) | 6 | 2 | 1 |
| Pleuritic pain | Additional description: Pleuritic pain | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sore throat | Additional description: Sore throat | | |
| subjects affected / exposed | 3 / 273 (1.10%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Pulmonary edema | Additional description: Pulmonary edema | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 2 / 273 (0.73%) | 2 / 272 (0.74%) |
| occurrences (all) | 2 | 2 | 2 |
| Pneumothorax | Additional description: Pneumothorax | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypoxia | Additional description: Hypoxia | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 2 / 272 (0.74%) |
| occurrences (all) | 0 | 1 | 2 |
| Dyspnea | Additional description: Dyspnea | | |
| subjects affected / exposed | 4 / 273 (1.47%) | 8 / 273 (2.93%) | 2 / 272 (0.74%) |
| occurrences (all) | 4 | 8 | 2 |
| Respiratory, thoracic and mediastinal disorders: Other, specify | Additional description: Respiratory, thoracic and mediastinal disorders: Other, specify | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 2 / 272 (0.74%) |
| occurrences (all) | 1 | 0 | 2 |
| Pharyngolarygeal pain | Additional description: Pharyngolarygeal pain | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Epistaxis | Additional description: Epistaxis | | |

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|--|--|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 3 / 273 (1.10%) 3 | 1 / 273 (0.37%) 1 | 2 / 272 (0.74%) 2 |
| Upper respiratory tract infection | Additional description: Upper respiratory tract infection | | |
| subjects affected / exposed occurrences (all) | 1 / 273 (0.37%) 1 | 0 / 273 (0.00%) 0 | 1 / 272 (0.37%) 1 |
| Productive cough | Additional description: Productive cough | | |
| subjects affected / exposed occurrences (all) | 2 / 273 (0.73%) 2 | 1 / 273 (0.37%) 1 | 0 / 272 (0.00%) 0 |
| Cough | Additional description: Cough | | |
| subjects affected / exposed occurrences (all) | 1 / 273 (0.37%) 1 | 2 / 273 (0.73%) 2 | 1 / 272 (0.37%) 1 |
| Bronchospasm | Additional description: Bronchospasm | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Psychiatric disorders | | | |
| Agitation | Additional description: Agitation | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 1 / 273 (0.37%) 1 | 1 / 272 (0.37%) 1 |
| Libido decreased | Additional description: Libido decreased | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Psychiatric disorders : Other, specify | Additional description: Psychiatric disorders : Other, specify | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 1 / 273 (0.37%) 1 | 0 / 272 (0.00%) 0 |
| Psychosis | Additional description: Psychosis | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 1 / 272 (0.37%) 1 |
| Hallucinations | Additional description: Hallucinations | | |
| subjects affected / exposed occurrences (all) | 4 / 273 (1.47%) 4 | 1 / 273 (0.37%) 1 | 1 / 272 (0.37%) 1 |
| Depression | Additional description: Depression | | |
| subjects affected / exposed occurrences (all) | 3 / 273 (1.10%) 3 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Confusion | Additional description: Confusion | | |
| subjects affected / exposed occurrences (all) | 3 / 273 (1.10%) 3 | 1 / 273 (0.37%) 1 | 3 / 272 (1.10%) 3 |

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|--|--|----------------------|----------------------|
| Suicide attempt subjects affected / exposed occurrences (all) | Additional description: Suicide attempt | | |
| | 1 / 273 (0.37%) 1 | 0 / 273 (0.00%) 0 | 1 / 272 (0.37%) 1 |
| Insomnia subjects affected / exposed occurrences (all) | Additional description: Insomnia | | |
| | 3 / 273 (1.10%) 3 | 3 / 273 (1.10%) 3 | 1 / 272 (0.37%) 1 |
| Investigations | | | |
| Alanine aminotranferase increased subjects affected / exposed occurrences (all) | Additional description: Alanine aminotranferase increased | | |
| | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Weight gain subjects affected / exposed occurrences (all) | Additional description: Weight gain | | |
| | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | Additional description: Aspartate aminotransferase increased | | |
| | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| INR increased subjects affected / exposed occurrences (all) | Additional description: INR increased | | |
| | 1 / 273 (0.37%) 1 | 0 / 273 (0.00%) 0 | 1 / 272 (0.37%) 1 |
| Leukocytosis subjects affected / exposed occurrences (all) | Additional description: Leukocytosis | | |
| | 1 / 273 (0.37%) 1 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Alkaline phosphatase increased subjects affected / exposed occurrences (all) | Additional description: Alkaline phosphatase increased | | |
| | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 2 / 272 (0.74%) 2 |
| White blood cell decreased subjects affected / exposed occurrences (all) | Additional description: White blood cell decreased | | |
| | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 2 / 272 (0.74%) 2 |
| Lymphocyte count increased subjects affected / exposed occurrences (all) | Additional description: Lymphocyte count increased | | |
| | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | Additional description: Blood bilirubin increased | | |
| | 0 / 273 (0.00%) 0 | 5 / 273 (1.83%) 5 | 4 / 272 (1.47%) 4 |
| Weight loss | Additional description: Weight loss | | |

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|--|--|-----------------|-----------------|
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalemia | Additional description: Hypokalemia | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Platelet count decreased | Additional description: Platelet count decreased | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alanine transferase increased | Additional description: Alanine transferase increased | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 2 / 272 (0.74%) |
| occurrences (all) | 1 | 0 | 2 |
| Cardiac troponin T increased | Additional description: Cardiac troponin T increased | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Investigations: Other, specify | Additional description: Investigations: Other, specify | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 2 / 273 (0.73%) | 3 / 272 (1.10%) |
| occurrences (all) | 2 | 2 | 3 |
| Serum amylase increased | Additional description: Serum amylase increased | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 2 / 273 (0.73%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Creatinine increased | Additional description: Creatinine increased | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 2 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| Spinal fracture | Additional description: Spinal fracture | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Fall | Additional description: Fall | | |
| subjects affected / exposed | 8 / 273 (2.93%) | 7 / 273 (2.56%) | 8 / 272 (2.94%) |
| occurrences (all) | 10 | 8 | 12 |
| Wound complication | Additional description: Wound complication | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Fracture | Additional description: Fracture | | |

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|--|--|-----------------|-----------------|
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infusion related reaction | Additional description: Infusion related reaction | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury to jugular vein | Additional description: Injury to jugular vein | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injury, poisoning and procedural complications: Other, specify | Additional description: Injury, poisoning and procedural complications: Other, specify | | |
| subjects affected / exposed | 3 / 273 (1.10%) | 2 / 273 (0.73%) | 3 / 272 (1.10%) |
| occurrences (all) | 3 | 2 | 3 |
| Sepsis | Additional description: Sepsis | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bruising | Additional description: Bruising | | |
| subjects affected / exposed | 3 / 273 (1.10%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Cardiac disorders | | | |
| Palpitations | Additional description: Palpitations | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Atrial fibrillation | Additional description: Atrial fibrillation | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 3 / 273 (1.10%) | 1 / 272 (0.37%) |
| occurrences (all) | 1 | 3 | 1 |
| Left ventricular systolic dysfunction | Additional description: Left ventricular systolic dysfunction | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders : Other, specify | Additional description: Cardiac disorders : Other, specify | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac arrest | Additional description: Cardiac arrest | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus tachycardia | Additional description: Sinus tachycardia | | |

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|--|--|-----------------|-----------------|
| subjects affected / exposed | 3 / 273 (1.10%) | 2 / 273 (0.73%) | 3 / 272 (1.10%) |
| occurrences (all) | 3 | 2 | 4 |
| Chest pain - cardiac | Additional description: Chest pain - cardiac | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Supraventricular tachycardia | Additional description: Supraventricular tachycardia | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Acute coronary syndrome | Additional description: Acute coronary syndrome | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cardiac disorders: Other, specify | Additional description: Cardiac disorders: Other, specify | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Depressed level of consciousness | Additional description: Depressed level of consciousness | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 4 / 272 (1.47%) |
| occurrences (all) | 1 | 0 | 4 |
| Syncope | Additional description: Syncope | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 1 | 1 |
| Seizure | Additional description: Seizure | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 1 | 0 | 1 |
| Tremor | Additional description: Tremor | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Nervous system disorders: Other, specify | Additional description: Nervous system disorders: Other, specify | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Psychiatric disorders: Other, specify | Additional description: Psychiatric disorders: Other, specify | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Encephalopathy | Additional description: Encephalopathy | | |

| | | | |
|--|--|-----------------|-----------------|
| subjects affected / exposed | 3 / 273 (1.10%) | 4 / 273 (1.47%) | 3 / 272 (1.10%) |
| occurrences (all) | 3 | 5 | 3 |
| Dizziness | Additional description: Dizziness | | |
| subjects affected / exposed | 3 / 273 (1.10%) | 2 / 273 (0.73%) | 0 / 272 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Headache | Additional description: Headache | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 5 / 273 (1.83%) | 4 / 272 (1.47%) |
| occurrences (all) | 2 | 6 | 4 |
| Dysphasia | Additional description: Dysphasia | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood and lymphatic system disorders | | | |
| Leukocytosis | Additional description: Leukocytosis | | |
| subjects affected / exposed | 4 / 273 (1.47%) | 2 / 273 (0.73%) | 3 / 272 (1.10%) |
| occurrences (all) | 4 | 4 | 3 |
| Blood and lymphatic system disorder : Other, specify | Additional description: Blood and lymphatic system disorder : Other, specify | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 2 / 272 (0.74%) |
| occurrences (all) | 0 | 0 | 2 |
| Anemia | Additional description: Anemia | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 2 / 273 (0.73%) | 5 / 272 (1.84%) |
| occurrences (all) | 2 | 2 | 6 |
| Ear and labyrinth disorders | | | |
| Ear pain | Additional description: Ear pain | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |
| Blurred vision | Additional description: Blurred vision | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye infection | Additional description: Eye infection | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal disorders | | | |
| Esophagitis | Additional description: Esophagitis | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|--|-----------------|------------------|
| Nausea | Additional description: Nausea | | |
| | 6 / 273 (2.20%) | 1 / 273 (0.37%) | 19 / 272 (6.99%) |
| subjects affected / exposed | 6 | 1 | 19 |
| occurrences (all) | | | |
| Bloating | Additional description: Bloating | | |
| | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| subjects affected / exposed | 0 | 0 | 0 |
| occurrences (all) | | | |
| Oral hemorrhage | Additional description: Oral hemorrhage | | |
| | 1 / 273 (0.37%) | 2 / 273 (0.73%) | 0 / 272 (0.00%) |
| subjects affected / exposed | 1 | 2 | 0 |
| occurrences (all) | | | |
| Gastrointestinal disorders: Other, specify | Additional description: Gastrointestinal disorders: Other, specify | | |
| | 3 / 273 (1.10%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| subjects affected / exposed | 3 | 0 | 1 |
| occurrences (all) | | | |
| Diarrhea | Additional description: Diarrhea | | |
| | 12 / 273 (4.40%) | 5 / 273 (1.83%) | 19 / 272 (6.99%) |
| subjects affected / exposed | 12 | 5 | 22 |
| occurrences (all) | | | |
| Esophageal varices hemorrhage | Additional description: Esophageal varices hemorrhage | | |
| | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 2 / 272 (0.74%) |
| subjects affected / exposed | 1 | 0 | 2 |
| occurrences (all) | | | |
| Gastritis | Additional description: Gastritis | | |
| | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| subjects affected / exposed | 0 | 1 | 0 |
| occurrences (all) | | | |
| Injury, poisoning and procedural complications: Other, specify | Additional description: Injury, poisoning and procedural complications: Other, specify | | |
| | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| subjects affected / exposed | 1 | 0 | 0 |
| occurrences (all) | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify | Additional description: Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify | | |
| | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| subjects affected / exposed | 0 | 0 | 1 |
| occurrences (all) | | | |
| Hemorrhoids | Additional description: Hemorrhoids | | |
| | 2 / 273 (0.73%) | 2 / 273 (0.73%) | 1 / 272 (0.37%) |
| subjects affected / exposed | 2 | 2 | 1 |
| occurrences (all) | | | |
| Duodenal ulcer | Additional description: Duodenal ulcer | | |
| | 1 / 273 (0.37%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| subjects affected / exposed | 1 | 1 | 0 |
| occurrences (all) | | | |
| Haemorrhoidal haemorrhage | Additional description: Haemorrhoidal haemorrhage | | |
| | | | |

| | | | |
|-----------------------------------|---|-----------------|------------------|
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal hemorrhage | Additional description: Rectal hemorrhage | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 0 / 273 (0.00%) | 2 / 272 (0.74%) |
| occurrences (all) | 2 | 0 | 2 |
| Upper gastrointestinal hemorrhage | Additional description: Upper gastrointestinal hemorrhage | | |
| subjects affected / exposed | 7 / 273 (2.56%) | 7 / 273 (2.56%) | 1 / 272 (0.37%) |
| occurrences (all) | 7 | 7 | 1 |
| Dry mouth | Additional description: Dry mouth | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Rectal pain | Additional description: Rectal pain | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastric ulcer | Additional description: Gastric ulcer | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain | Additional description: Abdominal pain | | |
| subjects affected / exposed | 14 / 273 (5.13%) | 8 / 273 (2.93%) | 11 / 272 (4.04%) |
| occurrences (all) | 15 | 11 | 12 |
| Dental caries | Additional description: Dental caries | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vomiting | Additional description: Vomiting | | |
| subjects affected / exposed | 9 / 273 (3.30%) | 5 / 273 (1.83%) | 13 / 272 (4.78%) |
| occurrences (all) | 11 | 5 | 16 |
| Enterocolitis infectious | Additional description: Enterocolitis infectious | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 3 / 273 (1.10%) | 1 / 272 (0.37%) |
| occurrences (all) | 1 | 3 | 1 |
| Esophageal perforation | Additional description: Esophageal perforation | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ileus | Additional description: Ileus | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 1 | 1 |
| Esophageal ulcer | Additional description: Esophageal ulcer | | |

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|-----------------------------------|---|------------------|------------------|
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Esophageal infection | Additional description: Esophageal infection | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ascites | Additional description: Ascites | | |
| subjects affected / exposed | 10 / 273 (3.66%) | 10 / 273 (3.66%) | 10 / 272 (3.68%) |
| occurrences (all) | 16 | 11 | 12 |
| Dysphagia | Additional description: Dysphagia | | |
| subjects affected / exposed | 4 / 273 (1.47%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 4 | 0 | 1 |
| Gastroesophageal reflux disease | Additional description: Gastroesophageal reflux disease | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal distension | Additional description: Abdominal distension | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 1 / 273 (0.37%) | 2 / 272 (0.74%) |
| occurrences (all) | 2 | 1 | 2 |
| Rectal stenosis | Additional description: Rectal stenosis | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Mucositis oral | Additional description: Mucositis oral | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lower gastrointestinal hemorrhage | Additional description: Lower gastrointestinal hemorrhage | | |
| subjects affected / exposed | 5 / 273 (1.83%) | 6 / 273 (2.20%) | 3 / 272 (1.10%) |
| occurrences (all) | 5 | 6 | 3 |
| Constipation | Additional description: Constipation | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 4 / 273 (1.47%) | 2 / 272 (0.74%) |
| occurrences (all) | 0 | 4 | 2 |
| Dyspepsia | Additional description: Dyspepsia | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Hepatobiliary disorders | | | |
| Hepatic failure | Additional description: Hepatic failure | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 2 / 273 (0.73%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

| | | | |
|--|--|----------------------|----------------------|
| Hepatobiliary disorders: Other, specify subjects affected / exposed occurrences (all) | Additional description: Hepatobiliary disorders: Other, specify | | |
| | 0 / 273 (0.00%) 0 | 1 / 273 (0.37%) 1 | 0 / 272 (0.00%) 0 |
| | | | |
| Biliary tract infection subjects affected / exposed occurrences (all) | Additional description: Biliary tract infection | | |
| | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 1 / 272 (0.37%) 1 |
| | | | |
| Portal hypertension subjects affected / exposed occurrences (all) | Additional description: Portal hypertension | | |
| | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| | | | |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis subjects affected / exposed occurrences (all) | Additional description: Hyperhidrosis | | |
| | 0 / 273 (0.00%) 0 | 1 / 273 (0.37%) 1 | 0 / 272 (0.00%) 0 |
| | | | |
| Rash maculo-papular subjects affected / exposed occurrences (all) | Additional description: Rash maculo-papular | | |
| | 6 / 273 (2.20%) 6 | 4 / 273 (1.47%) 4 | 7 / 272 (2.57%) 9 |
| | | | |
| Skin and subcutaneous tissue disorder : Other, specify subjects affected / exposed occurrences (all) | Additional description: Skin and subcutaneous tissue disorder : Other, specify | | |
| | 0 / 273 (0.00%) 0 | 2 / 273 (0.73%) 2 | 2 / 272 (0.74%) 2 |
| | | | |
| Pruritus subjects affected / exposed occurrences (all) | Additional description: Pruritus | | |
| | 7 / 273 (2.56%) 7 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| | | | |
| Alopecia subjects affected / exposed occurrences (all) | Additional description: Alopecia | | |
| | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| | | | |
| Papulopustular rash subjects affected / exposed occurrences (all) | Additional description: Papulopustular rash | | |
| | 0 / 273 (0.00%) 0 | 1 / 273 (0.37%) 1 | 0 / 272 (0.00%) 0 |
| | | | |
| Skin and subcutaneous tissue disorders: Other, specify subjects affected / exposed occurrences (all) | Additional description: Skin and subcutaneous tissue disorders: Other, specify | | |
| | 0 / 273 (0.00%) 0 | 1 / 273 (0.37%) 1 | 0 / 272 (0.00%) 0 |
| | | | |
| Erythema multiforme subjects affected / exposed occurrences (all) | Additional description: Erythema multiforme | | |
| | 1 / 273 (0.37%) 1 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| | | | |
| Skin ulceration | Additional description: Skin ulceration | | |
| | | | |

| | | | |
|---|---|-----------------|-----------------|
| subjects affected / exposed | 2 / 273 (0.73%) | 2 / 273 (0.73%) | 1 / 272 (0.37%) |
| occurrences (all) | 2 | 2 | 1 |
| Skin infection | Additional description: Skin infection | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Renal and urinary disorders | | | |
| Renal and urinary disorders: Other, specify | Additional description: Renal and urinary disorders: Other, specify | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 2 / 273 (0.73%) | 2 / 272 (0.74%) |
| occurrences (all) | 2 | 2 | 2 |
| Hematuria | Additional description: Hematuria | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 2 / 272 (0.74%) |
| occurrences (all) | 1 | 0 | 2 |
| Haematuria | Additional description: Haematuria | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chronic kidney disease | Additional description: Chronic kidney disease | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract pain | Additional description: Urinary tract pain | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 1 | 0 | 1 |
| Urinary tract infection | Additional description: Urinary tract infection | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Urinary tract obstruction | Additional description: Urinary tract obstruction | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Acute kidney injury | Additional description: Acute kidney injury | | |
| subjects affected / exposed | 5 / 273 (1.83%) | 0 / 273 (0.00%) | 4 / 272 (1.47%) |
| occurrences (all) | 6 | 0 | 4 |
| Endocrine disorders | | | |
| Endocrine disorders : Other, specify | Additional description: Endocrine disorders : Other, specify | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypothyroidism | Additional description: Hypothyroidism | | |

| | | | |
|---|---|----------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 1 / 273 (0.37%) 1 | 0 / 272 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Chest wall pain | Additional description: Chest wall pain | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Arthralgia | Additional description: Arthralgia | | |
| subjects affected / exposed occurrences (all) | 2 / 273 (0.73%) 2 | 0 / 273 (0.00%) 0 | 1 / 272 (0.37%) 1 |
| Back pain | Additional description: Back pain | | |
| subjects affected / exposed occurrences (all) | 6 / 273 (2.20%) 6 | 2 / 273 (0.73%) 2 | 2 / 272 (0.74%) 2 |
| Flank pain | Additional description: Flank pain | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 2 / 273 (0.73%) 2 | 0 / 272 (0.00%) 0 |
| Musculoskeletal and connective tissue disorder : Other, specify | Additional description: Musculoskeletal and connective tissue disorder : Other, specify | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 1 / 273 (0.37%) 1 | 0 / 272 (0.00%) 0 |
| Osteoporosis | Additional description: Osteoporosis | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 1 / 273 (0.37%) 1 | 0 / 272 (0.00%) 0 |
| Generalised muscle weakness | Additional description: Generalised muscle weakness | | |
| subjects affected / exposed occurrences (all) | 1 / 273 (0.37%) 1 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Arthralgia | Additional description: Arthralgia | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 1 / 272 (0.37%) 1 |
| Fracture | Additional description: Fracture | | |
| subjects affected / exposed occurrences (all) | 1 / 273 (0.37%) 1 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Pain in extremity | Additional description: Pain in extremity | | |
| subjects affected / exposed occurrences (all) | 3 / 273 (1.10%) 3 | 1 / 273 (0.37%) 1 | 1 / 272 (0.37%) 1 |
| Myalgia | Additional description: Myalgia | | |

| | | | |
|---|---|------------------------|----------------------|
| subjects affected / exposed occurrences (all) | 6 / 273 (2.20%) 6 | 2 / 273 (0.73%) 2 | 4 / 272 (1.47%) 5 |
| Infections and infestations | Additional description: Vaginal infection | | |
| Vaginal infection subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 1 / 273 (0.37%) 1 | 0 / 272 (0.00%) 0 |
| Hepatitis viral | Additional description: Hepatitis viral | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 1 / 273 (0.37%) 1 | 1 / 272 (0.37%) 1 |
| Sepsis | Additional description: Sepsis | | |
| subjects affected / exposed occurrences (all) | 3 / 273 (1.10%) 3 | 10 / 273 (3.66%) 13 | 4 / 272 (1.47%) 6 |
| Wound infection | Additional description: Wound infection | | |
| subjects affected / exposed occurrences (all) | 1 / 273 (0.37%) 1 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Mucosal infection | Additional description: Mucosal infection | | |
| subjects affected / exposed occurrences (all) | 3 / 273 (1.10%) 3 | 0 / 273 (0.00%) 0 | 2 / 272 (0.74%) 2 |
| Lung infection | Additional description: Lung infection | | |
| subjects affected / exposed occurrences (all) | 9 / 273 (3.30%) 9 | 10 / 273 (3.66%) 12 | 8 / 272 (2.94%) 8 |
| Esophageal infection | Additional description: Esophageal infection | | |
| subjects affected / exposed occurrences (all) | 0 / 273 (0.00%) 0 | 0 / 273 (0.00%) 0 | 1 / 272 (0.37%) 1 |
| Rash pustular | Additional description: Rash pustular | | |
| subjects affected / exposed occurrences (all) | 1 / 273 (0.37%) 1 | 0 / 273 (0.00%) 0 | 0 / 272 (0.00%) 0 |
| Urinary tract infection | Additional description: Urinary tract infection | | |
| subjects affected / exposed occurrences (all) | 11 / 273 (4.03%) 12 | 9 / 273 (3.30%) 9 | 7 / 272 (2.57%) 7 |
| Skin infection | Additional description: Skin infection | | |
| subjects affected / exposed occurrences (all) | 3 / 273 (1.10%) 3 | 6 / 273 (2.20%) 6 | 2 / 272 (0.74%) 2 |
| Infections and infestations: Other, specify | Additional description: Infections and infestations: Other, specify | | |

| | | | |
|---|---|-----------------|-----------------|
| subjects affected / exposed | 4 / 273 (1.47%) | 1 / 273 (0.37%) | 4 / 272 (1.47%) |
| occurrences (all) | 5 | 1 | 4 |
| Phlebitis infective | Additional description: Phlebitis infective | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 2 / 273 (0.73%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Metabolism and nutrition disorders | | | |
| Hypernatremia | Additional description: Hypernatremia | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 1 / 273 (0.37%) | 0 / 272 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| White blood cell decreased | Additional description: White blood cell decreased | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Dehydration | Additional description: Dehydration | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperglycemia | Additional description: Hyperglycemia | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 2 / 273 (0.73%) | 2 / 272 (0.74%) |
| occurrences (all) | 1 | 2 | 2 |
| Anorexia | Additional description: Anorexia | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 1 / 273 (0.37%) | 1 / 272 (0.37%) |
| occurrences (all) | 1 | 1 | 1 |
| Metabolism and nutrition disorders : Other, specify | Additional description: Metabolism and nutrition disorders : Other, specify | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 2 | 0 | 1 |
| Hypomagnesemia | Additional description: Hypomagnesemia | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 0 / 273 (0.00%) | 0 / 272 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Hyponatremia | Additional description: Hyponatremia | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 3 / 273 (1.10%) | 4 / 272 (1.47%) |
| occurrences (all) | 2 | 4 | 5 |
| Hypoalbuminemia | Additional description: Hypoalbuminemia | | |
| subjects affected / exposed | 2 / 273 (0.73%) | 1 / 273 (0.37%) | 2 / 272 (0.74%) |
| occurrences (all) | 2 | 1 | 2 |
| Hypophosphatemia | Additional description: Hypophosphatemia | | |

| | | | |
|-----------------------------|--------------------------------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 273 (0.73%) | 1 / 273 (0.37%) | 2 / 272 (0.74%) |
| occurrences (all) | 2 | 1 | 2 |
| Hypocalcemia | Additional description: Hypocalcemia | | |
| subjects affected / exposed | 0 / 273 (0.00%) | 0 / 273 (0.00%) | 3 / 272 (1.10%) |
| occurrences (all) | 0 | 0 | 4 |
| Hypokalemia | Additional description: Hypokalemia | | |
| subjects affected / exposed | 7 / 273 (2.56%) | 8 / 273 (2.93%) | 1 / 272 (0.37%) |
| occurrences (all) | 8 | 9 | 1 |
| Hyperkalemia | Additional description: Hyperkalemia | | |
| subjects affected / exposed | 1 / 273 (0.37%) | 0 / 273 (0.00%) | 1 / 272 (0.37%) |
| occurrences (all) | 1 | 0 | 1 |

| | | | |
|--|--|--|--|
| Non-serious adverse events | PTX/Pred. | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 91 / 274 (33.21%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps): Other, specify | Additional description: Neoplasms benign, malignant and unspecified (incl cysts and polyps): Other, specify | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify | Additional description: Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Vascular disorders | | | |
| Peripheral ischemia | Additional description: Peripheral ischemia | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vascular disorders : Other, specify | Additional description: Vascular disorders : Other, specify | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Hematoma | Additional description: Hematoma | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Hypotension | Additional description: Hypotension | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Thromboembolic event | Additional description: Thromboembolic event | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Fever | Additional description: Fever | | |
| subjects affected / exposed | 4 / 274 (1.46%) | | |
| occurrences (all) | 4 | | |
| General disorders and administration site conditions: Other, specify | Additional description: General disorders and administration site conditions: Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue | Additional description: Fatigue | | |
| subjects affected / exposed | 4 / 274 (1.46%) | | |
| occurrences (all) | 4 | | |
| Localised edema | Additional description: Localised edema | | |
| subjects affected / exposed | 4 / 274 (1.46%) | | |
| occurrences (all) | 4 | | |
| Hypothermia | Additional description: Hypothermia | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site reaction | Additional description: Injection site reaction | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Edema limbs | Additional description: Edema limbs | | |
| subjects affected / exposed | 7 / 274 (2.55%) | | |
| occurrences (all) | 7 | | |
| Infusion related reaction | Additional description: Infusion related reaction | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin infection | Additional description: Skin infection | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Malaise | Additional description: Malaise | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Facial pain | Additional description: Facial pain | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pruritus | Additional description: Pruritus | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Non-cardiac chest pain | Additional description: Non-cardiac chest pain | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Reproductive system and breast disorders | | | |
| Vaginal hemorrhage | Additional description: Vaginal hemorrhage | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Erectile dysfunction | Additional description: Erectile dysfunction | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gynecomastia | Additional description: Gynecomastia | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Reproductive system and breast disorders: Other, specify | Additional description: Reproductive system and breast disorders: Other, specify | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Reporoductive system and breast disorders : Other, specify | Additional description: Reporoductive system and breast disorders : Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | Additional description: Pleural effusion | | |
| subjects affected / exposed | 3 / 274 (1.09%) | | |
| occurrences (all) | 3 | | |
| Pleuritic pain | Additional description: Pleuritic pain | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | |
|---|---|--|
| Sore throat | Additional description: Sore throat | |
| subjects affected / exposed | 0 / 274 (0.00%) | |
| occurrences (all) | 0 | |
| Pulmonary edema | Additional description: Pulmonary edema | |
| subjects affected / exposed | 0 / 274 (0.00%) | |
| occurrences (all) | 0 | |
| Pneumothorax | Additional description: Pneumothorax | |
| subjects affected / exposed | 0 / 274 (0.00%) | |
| occurrences (all) | 0 | |
| Hypoxia | Additional description: Hypoxia | |
| subjects affected / exposed | 2 / 274 (0.73%) | |
| occurrences (all) | 2 | |
| Dyspnea | Additional description: Dyspnea | |
| subjects affected / exposed | 0 / 274 (0.00%) | |
| occurrences (all) | 0 | |
| Respiratory, thoracic and mediastinal disorders: Other, specify | Additional description: Respiratory, thoracic and mediastinal disorders: Other, specify | |
| subjects affected / exposed | 0 / 274 (0.00%) | |
| occurrences (all) | 0 | |
| Pharyngolaryngeal pain | Additional description: Pharyngolaryngeal pain | |
| subjects affected / exposed | 0 / 274 (0.00%) | |
| occurrences (all) | 0 | |
| Epistaxis | Additional description: Epistaxis | |
| subjects affected / exposed | 1 / 274 (0.36%) | |
| occurrences (all) | 1 | |
| Upper respiratory tract infection | Additional description: Upper respiratory tract infection | |
| subjects affected / exposed | 0 / 274 (0.00%) | |
| occurrences (all) | 0 | |
| Productive cough | Additional description: Productive cough | |
| subjects affected / exposed | 1 / 274 (0.36%) | |
| occurrences (all) | 1 | |
| Cough | Additional description: Cough | |
| subjects affected / exposed | 3 / 274 (1.09%) | |
| occurrences (all) | 3 | |
| Bronchospasm | Additional description: Bronchospasm | |

| | | | |
|--|--|--|--|
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Agitation | Additional description: Agitation | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Libido decreased | Additional description: Libido decreased | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders : Other, specify | Additional description: Psychiatric disorders : Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychosis | Additional description: Psychosis | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 2 | | |
| Hallucinations | Additional description: Hallucinations | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Depression | Additional description: Depression | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Confusion | Additional description: Confusion | | |
| subjects affected / exposed | 3 / 274 (1.09%) | | |
| occurrences (all) | 3 | | |
| Suicide attempt | Additional description: Suicide attempt | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Insomnia | Additional description: Insomnia | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Investigations | | | |
| Alanine aminotranferase increased | Additional description: Alanine aminotranferase increased | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Weight gain | Additional description: Weight gain | | |

| | | | |
|--------------------------------------|--|--|--|
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Aspartate aminotransferase increased | Additional description: Aspartate aminotransferase increased | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| INR increased | Additional description: INR increased | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Leukocytosis | Additional description: Leukocytosis | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Alkaline phosphatase increased | Additional description: Alkaline phosphatase increased | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| White blood cell decreased | Additional description: White blood cell decreased | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lymphocyte count increased | Additional description: Lymphocyte count increased | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Blood bilirubin increased | Additional description: Blood bilirubin increased | | |
| subjects affected / exposed | 6 / 274 (2.19%) | | |
| occurrences (all) | 6 | | |
| Weight loss | Additional description: Weight loss | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Hypokalemia | Additional description: Hypokalemia | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Platelet count decreased | Additional description: Platelet count decreased | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Alanine transferase increased | Additional description: Alanine transferase increased | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|--|--|--|
| Cardiac troponin T increased subjects affected / exposed occurrences (all) | Additional description: Cardiac troponin T increased | | |
| | 0 / 274 (0.00%) | | |
| | 0 | | |
| | Additional description: Investigations: Other, specify | | |
| Investigations: Other, specify subjects affected / exposed occurrences (all) | 1 / 274 (0.36%) | | |
| | 1 | | |
| | Additional description: Serum amylase increased | | |
| | 0 / 274 (0.00%) | | |
| Serum amylase increased subjects affected / exposed occurrences (all) | 0 | | |
| | Additional description: Creatinine increased | | |
| | 0 / 274 (0.00%) | | |
| | 0 | | |
| Creatinine increased subjects affected / exposed occurrences (all) | Additional description: Creatinine increased | | |
| | 0 / 274 (0.00%) | | |
| | 0 | | |
| | Additional description: Creatinine increased | | |
| Injury, poisoning and procedural complications Spinal fracture subjects affected / exposed occurrences (all) | Additional description: Spinal fracture | | |
| | 0 / 274 (0.00%) | | |
| | 0 | | |
| | Additional description: Fall | | |
| Fall subjects affected / exposed occurrences (all) | 7 / 274 (2.55%) | | |
| | 8 | | |
| | Additional description: Wound complication | | |
| | 0 / 274 (0.00%) | | |
| Wound complication subjects affected / exposed occurrences (all) | 0 | | |
| | Additional description: Fracture | | |
| | 1 / 274 (0.36%) | | |
| | 1 | | |
| Fracture subjects affected / exposed occurrences (all) | Additional description: Fracture | | |
| | 1 / 274 (0.36%) | | |
| | 1 | | |
| | Additional description: Infusion related reaction | | |
| Infusion related reaction subjects affected / exposed occurrences (all) | 0 / 274 (0.00%) | | |
| | 0 | | |
| | Additional description: Injury to jugular vein | | |
| | 0 / 274 (0.00%) | | |
| Injury to jugular vein subjects affected / exposed occurrences (all) | 0 | | |
| | Additional description: Injury, poisoning and procedural complications: Other, specify | | |
| | 3 / 274 (1.09%) | | |
| | 3 | | |
| Injury, poisoning and procedural complications: Other, specify subjects affected / exposed occurrences (all) | Additional description: Injury, poisoning and procedural complications: Other, specify | | |
| | 3 / 274 (1.09%) | | |
| | 3 | | |
| | Additional description: Sepsis | | |
| Sepsis | Additional description: Sepsis | | |
| | Additional description: Sepsis | | |
| | Additional description: Sepsis | | |
| | Additional description: Sepsis | | |

| | | | |
|---------------------------------------|---|--|--|
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bruising | Additional description: Bruising | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cardiac disorders | | | |
| Palpitations | Additional description: Palpitations | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Atrial fibrillation | Additional description: Atrial fibrillation | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Left ventricular systolic dysfunction | Additional description: Left ventricular systolic dysfunction | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cardiac disorders : Other, specify | Additional description: Cardiac disorders : Other, specify | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Cardiac arrest | Additional description: Cardiac arrest | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sinus tachycardia | Additional description: Sinus tachycardia | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Chest pain - cardiac | Additional description: Chest pain - cardiac | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Supraventricular tachycardia | Additional description: Supraventricular tachycardia | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Acute coronary syndrome | Additional description: Acute coronary syndrome | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cardiac disorders: Other, specify | Additional description: Cardiac disorders: Other, specify | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |

| | | | |
|--|--|--|--|
| Nervous system disorders | | | |
| Depressed level of consciousness | Additional description: Depressed level of consciousness | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Syncope | Additional description: Syncope | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Seizure | Additional description: Seizure | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Tremor | Additional description: Tremor | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders: Other, specify | Additional description: Nervous system disorders: Other, specify | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders: Other, specify | Additional description: Psychiatric disorders: Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Encephalopathy | Additional description: Encephalopathy | | |
| subjects affected / exposed | 4 / 274 (1.46%) | | |
| occurrences (all) | 5 | | |
| Dizziness | Additional description: Dizziness | | |
| subjects affected / exposed | 4 / 274 (1.46%) | | |
| occurrences (all) | 4 | | |
| Headache | Additional description: Headache | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dysphasia | Additional description: Dysphasia | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| Leukocytosis | Additional description: Leukocytosis | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorder : Other, specify | Additional description: Blood and lymphatic system disorder : Other, specify | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Anemia | Additional description: Anemia | | |
| subjects affected / exposed | 3 / 274 (1.09%) | | |
| occurrences (all) | 3 | | |
| Ear and labyrinth disorders | | | |
| Ear pain | Additional description: Ear pain | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye disorders | | | |
| Blurred vision | Additional description: Blurred vision | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye infection | Additional description: Eye infection | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Esophagitis | Additional description: Esophagitis | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Nausea | Additional description: Nausea | | |
| subjects affected / exposed | 8 / 274 (2.92%) | | |
| occurrences (all) | 8 | | |
| Bloating | Additional description: Bloating | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Oral hemorrhage | Additional description: Oral hemorrhage | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders: Other, specify | Additional description: Gastrointestinal disorders: Other, specify | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Diarrhea | Additional description: Diarrhea | | |
| subjects affected / exposed | 8 / 274 (2.92%) | | |
| occurrences (all) | 9 | | |
| Esophageal varices hemorrhage | Additional description: Esophageal varices hemorrhage | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed | 3 / 274 (1.09%) | | |
| occurrences (all) | 4 | | |
| Gastritis | Additional description: Gastritis | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injury, poisoning and procedural complications: Other, specify | Additional description: Injury, poisoning and procedural complications: Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify | Additional description: Neoplasms benign, malignant and unspecified (incl cysts and polyps) : Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hemorrhoids | Additional description: Hemorrhoids | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Duodenal ulcer | Additional description: Duodenal ulcer | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haemorrhoidal haemorrhage | Additional description: Haemorrhoidal haemorrhage | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Rectal hemorrhage | Additional description: Rectal hemorrhage | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Upper gastrointestinal hemorrhage | Additional description: Upper gastrointestinal hemorrhage | | |
| subjects affected / exposed | 4 / 274 (1.46%) | | |
| occurrences (all) | 6 | | |
| Dry mouth | Additional description: Dry mouth | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Rectal pain | Additional description: Rectal pain | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Gastric ulcer | Additional description: Gastric ulcer | | |

| | | | |
|---------------------------------|---|--|--|
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain | Additional description: Abdominal pain | | |
| subjects affected / exposed | 6 / 274 (2.19%) | | |
| occurrences (all) | 8 | | |
| Dental caries | Additional description: Dental caries | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vomiting | Additional description: Vomiting | | |
| subjects affected / exposed | 11 / 274 (4.01%) | | |
| occurrences (all) | 12 | | |
| Enterocolitis infectious | Additional description: Enterocolitis infectious | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Esophageal perforation | Additional description: Esophageal perforation | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ileus | Additional description: Ileus | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Esophageal ulcer | Additional description: Esophageal ulcer | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Esophageal infection | Additional description: Esophageal infection | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ascites | Additional description: Ascites | | |
| subjects affected / exposed | 11 / 274 (4.01%) | | |
| occurrences (all) | 14 | | |
| Dysphagia | Additional description: Dysphagia | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Gastroesophageal reflux disease | Additional description: Gastroesophageal reflux disease | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal distension | Additional description: Abdominal distension | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Rectal stenosis | Additional description: Rectal stenosis | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Mucositis oral | Additional description: Mucositis oral | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Lower gastrointestinal hemorrhage | Additional description: Lower gastrointestinal hemorrhage | | |
| subjects affected / exposed | 7 / 274 (2.55%) | | |
| occurrences (all) | 8 | | |
| Constipation | Additional description: Constipation | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Dyspepsia | Additional description: Dyspepsia | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Hepatobiliary disorders | | | |
| Hepatic failure | Additional description: Hepatic failure | | |
| subjects affected / exposed | 3 / 274 (1.09%) | | |
| occurrences (all) | 3 | | |
| Hepatobiliary disorders: Other, specify | Additional description: Hepatobiliary disorders: Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Biliary tract infection | Additional description: Biliary tract infection | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Portal hypertension | Additional description: Portal hypertension | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis | Additional description: Hyperhidrosis | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash maculo-papular | Additional description: Rash maculo-papular | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed | 8 / 274 (2.92%) | | |
| occurrences (all) | 9 | | |
| Skin and subcutaneous tissue disorder : Other, specify | Additional description: Skin and subcutaneous tissue disorder : Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pruritus | Additional description: Pruritus | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Alopecia | Additional description: Alopecia | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Papulopustular rash | Additional description: Papulopustular rash | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders: Other, specify | Additional description: Skin and subcutaneous tissue disorders: Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Erythema multiforme | Additional description: Erythema multiforme | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin ulceration | Additional description: Skin ulceration | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Skin infection | Additional description: Skin infection | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Renal and urinary disorders | Additional description: Renal and urinary disorders: Other, specify | | |
| Renal and urinary disorders: Other, specify | Additional description: Renal and urinary disorders: Other, specify | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Hematuria | Additional description: Hematuria | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haematuria | Additional description: Haematuria | | |

| | | | |
|---|--|--|--|
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chronic kidney disease | Additional description: Chronic kidney disease | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Urinary tract pain | Additional description: Urinary tract pain | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Urinary tract infection | Additional description: Urinary tract infection | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary tract obstruction | Additional description: Urinary tract obstruction | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Acute kidney injury | Additional description: Acute kidney injury | | |
| subjects affected / exposed | 3 / 274 (1.09%) | | |
| occurrences (all) | 3 | | |
| Endocrine disorders | | | |
| Endocrine disorders : Other, specify | Additional description: Endocrine disorders : Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypothyroidism | Additional description: Hypothyroidism | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Chest wall pain | Additional description: Chest wall pain | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Arthralgia | Additional description: Arthralgia | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Back pain | Additional description: Back pain | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Flank pain | Additional description: Flank pain | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorder : Other, specify | Additional description: Musculoskeletal and connective tissue disorder : Other, specify | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Osteoporosis | Additional description: Osteoporosis | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Generalised muscle weakness | Additional description: Generalised muscle weakness | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Arthralgia | Additional description: Arthralgia | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fracture | Additional description: Fracture | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain in extremity | Additional description: Pain in extremity | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myalgia | Additional description: Myalgia | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Infections and infestations | | | |
| Vaginal infection | Additional description: Vaginal infection | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hepatitis viral | Additional description: Hepatitis viral | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sepsis | Additional description: Sepsis | | |
| subjects affected / exposed | 7 / 274 (2.55%) | | |
| occurrences (all) | 8 | | |
| Wound infection | Additional description: Wound infection | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Mucosal infection | Additional description: Mucosal infection | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Lung infection | Additional description: Lung infection | | |
| subjects affected / exposed | 13 / 274 (4.74%) | | |
| occurrences (all) | 15 | | |
| Esophageal infection | Additional description: Esophageal infection | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Rash pustular | Additional description: Rash pustular | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary tract infection | Additional description: Urinary tract infection | | |
| subjects affected / exposed | 4 / 274 (1.46%) | | |
| occurrences (all) | 5 | | |
| Skin infection | Additional description: Skin infection | | |
| subjects affected / exposed | 4 / 274 (1.46%) | | |
| occurrences (all) | 4 | | |
| Infections and infestations: Other, specify | Additional description: Infections and infestations: Other, specify | | |
| subjects affected / exposed | 5 / 274 (1.82%) | | |
| occurrences (all) | 5 | | |
| Phlebitis infective | Additional description: Phlebitis infective | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |
| Hypernatremia | Additional description: Hypernatremia | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| White blood cell decreased | Additional description: White blood cell decreased | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dehydration | Additional description: Dehydration | | |

| | | | |
|--|---|--|--|
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperglycemia | Additional description: Hyperglycemia | | |
| subjects affected / exposed | 1 / 274 (0.36%) | | |
| occurrences (all) | 1 | | |
| Anorexia | Additional description: Anorexia | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Metabolism and nutrition disorders : Other, specify | Additional description: Metabolism and nutrition disorders : Other, specify | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypomagnesemia | Additional description: Hypomagnesemia | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Hyponatremia | Additional description: Hyponatremia | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypoalbuminemia | Additional description: Hypoalbuminemia | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 2 | | |
| Hypophosphatemia | Additional description: Hypophosphatemia | | |
| subjects affected / exposed | 3 / 274 (1.09%) | | |
| occurrences (all) | 3 | | |
| Hypocalcemia | Additional description: Hypocalcemia | | |
| subjects affected / exposed | 2 / 274 (0.73%) | | |
| occurrences (all) | 3 | | |
| Hypokalemia | Additional description: Hypokalemia | | |
| subjects affected / exposed | 4 / 274 (1.46%) | | |
| occurrences (all) | 4 | | |
| Hyperkalemia | Additional description: Hyperkalemia | | |
| subjects affected / exposed | 0 / 274 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25901427>

<http://www.ncbi.nlm.nih.gov/pubmed/26691209>