



Clinical trial results:

A Multi-indication, Single-treatment Arm, Open-label Phase 2 Study of Regorafenib and Nivolumab in Combination in Patients with Recurrent or Metastatic Solid Tumors

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2020-003359-13 |
| Trial protocol | GB FR BE IT |
| Global end of trial date | 29 March 2024 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 05 April 2025 |
| First version publication date | 05 April 2025 |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | BAY73-4506/21136 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04704154 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Bayer AG |
| Sponsor organisation address | Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368 |
| Public contact | Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com |
| Scientific contact | Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 07 October 2024 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|---------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 29 March 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate efficacy of the regorafenib and nivolumab combination by cohort

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects (or their legally authorized representative according to local legislation). Participating subjects (or their legally authorized representative according to local legislation) signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 03 February 2021 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Safety |
| Long term follow-up duration | 1 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Belgium: 14 |
| Country: Number of subjects enrolled | France: 46 |
| Country: Number of subjects enrolled | Italy: 30 |
| Country: Number of subjects enrolled | Japan: 29 |
| Country: Number of subjects enrolled | Korea, Republic of: 22 |
| Country: Number of subjects enrolled | Taiwan: 14 |
| Country: Number of subjects enrolled | United Kingdom: 8 |
| Country: Number of subjects enrolled | United States: 12 |
| Worldwide total number of subjects | 175 |
| EEA total number of subjects | 90 |

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) | 95 |
| From 65 to 84 years | 80 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 34 study centers in 8 countries/regions (6 centers in France, 5 centers in Italy, 2 centers in South Korea, 3 centers in Taiwan, 4 centers in the United Kingdom, 5 centers in Japan, 6 centers in the US and 3 centers in Belgium) from 03 February 2021 (first patient first visit) to 29 March 2024 (last patient last visit)

Pre-assignment

Screening details:

175 participants were enrolled and received study treatment. Participants were enrolled in 6 cohorts: HNSCC IO naïve (N=30), HNSCC IO treated (N=20), ESCC (N=30), PDAC (N=20), BTC (N=45), and GBM/AA (N=30)

Period 1

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

Arms

| | |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | HNSCC (IO naïve) |

Arm description:

Participants with confirmed recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) without Immune-oncology (IO), received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | Opdivo |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

480 mg administered on Day 1 of each treatment cycle.

| | |
|--|-------------|
| Investigational medicinal product name | Regorafenib |
| Investigational medicinal product code | BAY73-4506 |
| Other name | Stivarga |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Intake orally, starting with 3x 30 mg tablets every day (once daily.) for 21 days of every 28-day cycle (21 days on, 7 days off). If the starting dose is well tolerated dose can be escalated to 120 mg (4x30 mg tablets).

| | |
|------------------|--------------------|
| Arm title | HNSCC (IO treated) |
|------------------|--------------------|

Arm description:

Participants with confirmed recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) and with Immune-oncology (IO) treated, received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

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

| | |
|--|-----------------------|
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | Opdivo |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

480 mg administered on Day 1 of each treatment cycle.

| | |
|--|-------------|
| Investigational medicinal product name | Regorafenib |
| Investigational medicinal product code | BAY73-4506 |
| Other name | Stivarga |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Intake orally, starting with 3x 30 mg tablets every day (once daily.) for 21 days of every 28-day cycle (21 days on, 7 days off). If the starting dose is well tolerated dose can be escalated to 120 mg (4x30 mg tablets).

| | |
|------------------|------|
| Arm title | ESCC |
|------------------|------|

Arm description:

Participants with confirmed recurrent or metastatic Esophageal Squamous Cell Carcinoma (ESCC) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | Opdivo |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

480 mg administered on Day 1 of each treatment cycle.

| | |
|--|-------------|
| Investigational medicinal product name | Regorafenib |
| Investigational medicinal product code | BAY73-4506 |
| Other name | Stivarga |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Intake orally, starting with 3x 30 mg tablets every day (once daily.) for 21 days of every 28-day cycle (21 days on, 7 days off). If the starting dose is well tolerated dose can be escalated to 120 mg (4x30 mg tablets).

| | |
|------------------|------|
| Arm title | PDAC |
|------------------|------|

Arm description:

Participants with confirmed recurrent or metastatic Pancreatic Duct Adenocarcinoma (PDAC) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Regorafenib |
| Investigational medicinal product code | BAY73-4506 |
| Other name | Stivarga |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Intake orally, starting with 3x 30 mg tablets every day (once daily.) for 21 days of every 28-day cycle (21 days on, 7 days off). If the starting dose is well tolerated dose can be escalated to 120 mg (4x30

mg tablets).

| | |
|--|-----------------------|
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | Opdivo |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

480 mg administered on Day 1 of each treatment cycle.

| | |
|------------------|----------------------------|
| Arm title | Biliary Tract Cancer (BTC) |
|------------------|----------------------------|

Arm description:

Participants with confirmed recurrent or metastatic BTC received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Regorafenib |
| Investigational medicinal product code | BAY73-4506 |
| Other name | Stivarga |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Intake orally, starting with 3x 30 mg tablets every day (once daily.) for 21 days of every 28-day cycle (21 days on, 7 days off). If the starting dose is well tolerated dose can be escalated to 120 mg (4x30 mg tablets).

| | |
|--|-----------------------|
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | Opdivo |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

480 mg administered on Day 1 of each treatment cycle.

| | |
|------------------|--------|
| Arm title | GBM/AA |
|------------------|--------|

Arm description:

Participants with Glioblastoma Multiforme (GBM) or Anaplastic Astrocytoma (AA) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | Opdivo |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

480 mg administered on Day 1 of each treatment cycle.

| | |
|--|-------------|
| Investigational medicinal product name | Regorafenib |
| Investigational medicinal product code | BAY73-4506 |
| Other name | Stivarga |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Intake orally, starting with 3x 30 mg tablets every day (once daily.) for 21 days of every 28-day cycle (21 days on, 7 days off). If the starting dose is well tolerated dose can be escalated to 120 mg (4x30 mg tablets).

| Number of subjects in period 1 | HNSCC (IO naive) | HNSCC (IO treated) | ESCC |
|---|------------------|--------------------|------|
| Started | 30 | 20 | 30 |
| Completed | 0 | 0 | 0 |
| Not completed | 30 | 20 | 30 |
| Adverse event, serious fatal | 3 | - | - |
| Participant Decision | 1 | 1 | - |
| Completed max 24 infusions of Nivolumab | 2 | - | 1 |
| Physician decision | 1 | - | 1 |
| Adverse event, non-fatal | 3 | 2 | 4 |
| Progressive Disease | 19 | 17 | 20 |
| Continued in rollover study for regorafenib | 1 | - | 4 |

| Number of subjects in period 1 | PDAC | Biliary Tract Cancer (BTC) | GBM/AA |
|---|------|----------------------------|--------|
| Started | 20 | 45 | 30 |
| Completed | 0 | 0 | 0 |
| Not completed | 20 | 45 | 30 |
| Adverse event, serious fatal | - | 3 | - |
| Participant Decision | - | - | - |
| Completed max 24 infusions of Nivolumab | - | 1 | - |
| Physician decision | - | 2 | - |
| Adverse event, non-fatal | 2 | 3 | - |
| Progressive Disease | 18 | 36 | 30 |
| Continued in rollover study for regorafenib | - | - | - |

Baseline characteristics

Reporting groups

| | |
|---|----------------------------|
| Reporting group title | HNSCC (IO naive) |
| Reporting group description: Participants with confirmed recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) without Immune-oncology (IO), received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated. | |
| Reporting group title | HNSCC (IO treated) |
| Reporting group description: Participants with confirmed recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) and with Immune-oncology (IO) treated, received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated. | |
| Reporting group title | ESCC |
| Reporting group description: Participants with confirmed recurrent or metastatic Esophageal Squamous Cell Carcinoma (ESCC) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated. | |
| Reporting group title | PDAC |
| Reporting group description: Participants with confirmed recurrent or metastatic Pancreatic Duct Adenocarcinoma (PDAC) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated. | |
| Reporting group title | Biliary Tract Cancer (BTC) |
| Reporting group description: Participants with confirmed recurrent or metastatic BTC received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated. | |
| Reporting group title | GBM/AA |
| Reporting group description: Participants with Glioblastoma Multiforme (GBM) or Anaplastic Astrocytoma (AA) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated. | |

| Reporting group values | HNSCC (IO naive) | HNSCC (IO treated) | ESCC |
|---------------------------------------|------------------|--------------------|----------|
| Number of subjects | 30 | 20 | 30 |
| Age Categorical Units: Subjects | | | |
| Adults (18-64 years) | 16 | 10 | 17 |
| From 65-84 years | 14 | 10 | 13 |
| Age Continuous Units: years | | | |
| median | 63.0 | 64.5 | 62.0 |
| full range (min-max) | 26 to 76 | 44 to 81 | 49 to 76 |
| Gender Categorical Units: Subjects | | | |
| Female | 5 | 6 | 3 |
| Male | 25 | 14 | 27 |

| | | | |
|---------------------------|----|----|----|
| Race | | | |
| Units: Subjects | | | |
| Asian | 15 | 11 | 21 |
| Black or African American | 0 | 0 | 0 |
| White | 6 | 6 | 7 |
| Not Reported | 9 | 3 | 2 |

| Reporting group values | PDAC | Biliary Tract Cancer (BTC) | GBM/AA |
|---------------------------|----------|----------------------------|----------|
| Number of subjects | 20 | 45 | 30 |
| Age Categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 13 | 17 | 22 |
| From 65-84 years | 7 | 28 | 8 |
| Age Continuous | | | |
| Units: years | | | |
| median | 57.0 | 67.0 | 59.5 |
| full range (min-max) | 42 to 74 | 32 to 81 | 21 to 75 |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 11 | 20 | 10 |
| Male | 9 | 25 | 20 |
| Race | | | |
| Units: Subjects | | | |
| Asian | 5 | 11 | 2 |
| Black or African American | 0 | 1 | 0 |
| White | 13 | 27 | 26 |
| Not Reported | 2 | 6 | 2 |

| Reporting group values | Total | | |
|---------------------------|-------|--|--|
| Number of subjects | 175 | | |
| Age Categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 95 | | |
| From 65-84 years | 80 | | |
| Age Continuous | | | |
| Units: years | | | |
| median | | | |
| full range (min-max) | - | | |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 55 | | |
| Male | 120 | | |
| Race | | | |
| Units: Subjects | | | |
| Asian | 65 | | |
| Black or African American | 1 | | |
| White | 85 | | |
| Not Reported | 24 | | |

Subject analysis sets

| | |
|----------------------------|-------------------------|
| Subject analysis set title | FAS (full analysis set) |
| Subject analysis set type | Full analysis |

Subject analysis set description:

All participants who have received any dose of study intervention

| | |
|----------------------------|---------------------------|
| Subject analysis set title | SAF (safety analysis set) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All participants who have received any dose of study intervention. As the safety analysis set equals the full analysis, all safety related analysis were performed on the full analysis set.

| Reporting group values | FAS (full analysis set) | SAF (safety analysis set) | |
|--|-------------------------|---------------------------|--|
| Number of subjects | 175 | 175 | |
| Age Categorical Units: Subjects | | | |
| Adults (18-64 years) | 95 | 95 | |
| From 65-84 years | 80 | 80 | |
| Age Continuous Units: years median full range (min-max) | | | |
| Gender Categorical Units: Subjects | | | |
| Female | 55 | 55 | |
| Male | 120 | 120 | |
| Race Units: Subjects | | | |
| Asian | 65 | 65 | |
| Black or African American | 1 | 1 | |
| White | 85 | 85 | |
| Not Reported | 24 | 24 | |

End points

End points reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | HNSCC (IO naive) |
|-----------------------|------------------|

Reporting group description:

Participants with confirmed recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) without Immune-oncology (IO), received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

| | |
|-----------------------|--------------------|
| Reporting group title | HNSCC (IO treated) |
|-----------------------|--------------------|

Reporting group description:

Participants with confirmed recurrent or metastatic Head and Neck Squamous Cell Carcinoma (HNSCC) and with Immune-oncology (IO) treated, received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

| | |
|-----------------------|------|
| Reporting group title | ESCC |
|-----------------------|------|

Reporting group description:

Participants with confirmed recurrent or metastatic Esophageal Squamous Cell Carcinoma (ESCC) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

| | |
|-----------------------|------|
| Reporting group title | PDAC |
|-----------------------|------|

Reporting group description:

Participants with confirmed recurrent or metastatic Pancreatic Duct Adenocarcinoma (PDAC) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

| | |
|-----------------------|----------------------------|
| Reporting group title | Biliary Tract Cancer (BTC) |
|-----------------------|----------------------------|

Reporting group description:

Participants with confirmed recurrent or metastatic BTC received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

| | |
|-----------------------|--------|
| Reporting group title | GBM/AA |
|-----------------------|--------|

Reporting group description:

Participants with Glioblastoma Multiforme (GBM) or Anaplastic Astrocytoma (AA) received 480 mg nivolumab intravenously on day 1 of every treatment cycle. Regorafenib was given as 30 mg tablets daily (QD) for 3 weeks of each treatment cycle (28 days cycle length) with a starting dose of 90 mg that could be escalated to 120 mg if well tolerated.

| | |
|----------------------------|-------------------------|
| Subject analysis set title | FAS (full analysis set) |
|----------------------------|-------------------------|

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

Subject analysis set description:

All participants who have received any dose of study intervention

| | |
|----------------------------|---------------------------|
| Subject analysis set title | SAF (safety analysis set) |
|----------------------------|---------------------------|

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

Subject analysis set description:

All participants who have received any dose of study intervention. As the safety analysis set equals the full analysis, all safety related analysis were performed on the full analysis set.

Primary: Overall response rate (ORR)

| | |
|-----------------|--|
| End point title | Overall response rate (ORR) ^[1] |
|-----------------|--|

End point description:

Tumor response was evaluated as ORR per RECIST 1.1 by local assessments for all tumor types, except for GBM/AA, where ORR per RANO by local assessment was used. ORR was defined as the proportion of participants with best overall response of complete response (CR) or partial response (PR). Participants for whom best overall tumor response was not CR or PR, as well as participants without any post-baseline tumor assessment were considered non-responders. Descriptive statistics were done, no

inferential statistical analyses were performed

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

End point timeframe:

From first participant enrolled to cut-off date (ie after the last participant has been followed for approximately 10 months) approximately 26 months

Notes:

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

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values | HNSCC (IO naive) | HNSCC (IO treated) | ESCC | PDAC |
|-----------------------------|------------------|--------------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 30 | 20 | 30 | 20 |
| Units: Subjects | | | | |
| Overall Response Rate (ORR) | 6 | 1 | 15 | 0 |

| End point values | Biliary Tract Cancer (BTC) | GBM/AA | | |
|-----------------------------|----------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 30 | | |
| Units: Subjects | | | | |
| Overall Response Rate (ORR) | 2 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR)

| | |
|-----------------|----------------------------|
| End point title | Duration of response (DOR) |
|-----------------|----------------------------|

End point description:

Defined as the time (in days) from the first documented objective response of PR or CR, whichever is noted earlier, to disease progression or death (if death occurs before progression is documented). DOR will be defined for responders only, i.e. participants with a CR or PR.

99999: Value cannot be estimated due to censored data, insufficient number of participants with events.

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

End point timeframe:

From first participant enrolled to cut-off date (ie after the last participant has been followed for approximately 10 months) approximately 26 months

| End point values | HNSCC (IO naive) | HNSCC (IO treated) | ESCC | PDAC |
|----------------------------------|----------------------|------------------------|-------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 6 ^[2] | 1 ^[3] | 15 ^[4] | 0 ^[5] |
| Units: Days | | | | |
| median (confidence interval 80%) | | | | |
| DOR Median [80% CI] | 99999 (654 to 99999) | 99999 (99999 to 99999) | 420 (112 to 617) | (to) |

Notes:

[2] - Subgroup of participants with best overall response of CR or PR who received the study treatment

[3] - Subgroup of participants with best overall response of CR or PR who received the study treatment

[4] - Subgroup of participants with best overall response of CR or PR who received the study treatment

[5] - Subgroup of participants with best overall response of CR or PR who received the study treatment

| End point values | Biliary Tract Cancer (BTC) | GBM/AA | | |
|----------------------------------|----------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 2 ^[6] | 1 ^[7] | | |
| Units: Days | | | | |
| median (confidence interval 80%) | | | | |
| DOR Median [80% CI] | 432 (112 to 99999) | 140 (-99999 to 99999) | | |

Notes:

[6] - Subgroup of participants with best overall response of CR or PR who received the study treatment

[7] - Subgroup of participants with best overall response of CR or PR who received the study treatment

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate (DCR)

| | |
|-----------------|----------------------------|
| End point title | Disease control rate (DCR) |
|-----------------|----------------------------|

End point description:

CR = Complete response; PR = Partial response; SD = Stable disease

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

End point timeframe:

From first participant enrolled to cut-off date (ie after the last participant has been followed for approximately 10 months) approximately 26 months

| End point values | HNSCC (IO naive) | HNSCC (IO treated) | ESCC | PDAC |
|---|------------------|--------------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 30 | 20 | 30 | 20 |
| Units: Subjects | | | | |
| Disease Control Rate (DCR) CR, PR or SD | 16 | 13 | 22 | 7 |

| End point values | Biliary Tract Cancer (BTC) | GBM/AA | | |
|------------------|----------------------------|--------|--|--|
|------------------|----------------------------|--------|--|--|

| | | | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 30 | | |
| Units: Subjects | | | | |
| Disease Control Rate (DCR) CR, PR or SD | 24 | 10 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS)

| | |
|---|---------------------------------|
| End point title | Progression free survival (PFS) |
| End point description: | |
| PFS was defined as the time (in days) from the start of study intervention to the date of first objectively documented progressive disease (PD) or death from any cause (if no progression was documented). | |
| End point type | Secondary |
| End point timeframe: | |
| From first participant enrolled to cut-off date (ie after the last participant has been followed for approximately 10 months) approximately 26 months | |

| End point values | HNSCC (IO naive) | HNSCC (IO treated) | ESCC | PDAC |
|---|------------------|--------------------|------------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 30 | 20 | 30 | 20 |
| Units: Days | | | | |
| median (confidence interval 80%) | | | | |
| Progression Free Survival (PFS) Median [80% CI] | 79 (50 to 227) | 105 (52 to 115) | 259 (110 to 472) | 53 (48 to 111) |

| End point values | Biliary Tract Cancer (BTC) | GBM/AA | | |
|---|----------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 30 | | |
| Units: Days | | | | |
| median (confidence interval 80%) | | | | |
| Progression Free Survival (PFS) Median [80% CI] | 98 (55 to 112) | 55 (52 to 84) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: 6 months PFS

| | |
|--|--------------|
| End point title | 6 months PFS |
| End point description: | |
| 6 Months PFS rate | |
| End point type | Secondary |
| End point timeframe: | |
| Up to last participant follow 6 months (approximately 22 months) | |

| End point values | HNSCC (IO naive) | HNSCC (IO treated) | ESCC | PDAC |
|---|------------------------|------------------------|------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 30 | 20 | 30 | 20 |
| Units: Proportion of participants | | | | |
| number (confidence interval 80%) | | | | |
| Progression-free survival rate at month 6 | 0.455 (0.337 to 0.573) | 0.263 (0.134 to 0.393) | 0.533 (0.417 to 0.650) | 0.050 (0.000 to 0.112) |

| End point values | Biliary Tract Cancer (BTC) | GBM/AA | | |
|---|----------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 30 | | |
| Units: Proportion of participants | | | | |
| number (confidence interval 80%) | | | | |
| Progression-free survival rate at month 6 | 0.148 (0.077 to 0.218) | 0.167 (0.079 to 0.254) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

| | |
|---|-----------------------|
| End point title | Overall survival (OS) |
| End point description: | |
| OS was defined as the time (in days) from the start of study intervention to the date of death due to any cause. | |
| End point type | Secondary |
| End point timeframe: | |
| From first participant enrolled to cut-off date (ie after the last participant has been followed for approximately 10 months) approximately 26 months | |

| End point values | HNSCC (IO naive) | HNSCC (IO treated) | ESCC | PDAC |
|----------------------------------|------------------|--------------------|------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 30 | 20 | 30 | 20 |
| Units: Days | | | | |
| median (confidence interval 80%) | | | | |
| Overall Survival Median [80% CI] | 358 (198 to 418) | 355 (126 to 614) | 627 (431 to 865) | 259 (134 to 311) |

| End point values | Biliary Tract Cancer (BTC) | GBM/AA | | |
|----------------------------------|----------------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 30 | | |
| Units: Days | | | | |
| median (confidence interval 80%) | | | | |
| Overall Survival Median [80% CI] | 246 (176 to 386) | 245 (127 to 377) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: 1 year OS

| | |
|-----------------|-----------|
| End point title | 1 year OS |
|-----------------|-----------|

End point description:

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

End point timeframe:

From first participant enrolled to cut-off date (ie after the last participant has been followed for approximately 10 months) approximately 26 month

| End point values | HNSCC (IO naive) | HNSCC (IO treated) | ESCC | PDAC |
|-----------------------------------|------------------------|------------------------|------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 30 | 20 | 30 | 20 |
| Units: Proportion of patients | | | | |
| number (confidence interval 80%) | | | | |
| Overall survival rate at month 12 | 0.415 (0.298 to 0.532) | 0.444 (0.294 to 0.595) | 0.764 (0.664 to 0.864) | 0.281 (0.145 to 0.418) |

| End point values | Biliary Tract Cancer (BTC) | GBM/AA | | |
|-----------------------------|----------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 30 | | |

| | | | | |
|-----------------------------------|------------------------|------------------------|--|--|
| Units: Proportion of patients | | | | |
| number (confidence interval 80%) | | | | |
| Overall survival rate at month 12 | 0.422 (0.323 to 0.521) | 0.337 (0.223 to 0.451) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events

| | |
|--|--|
| End point title | Number of participants with adverse events |
| End point description: | |
| AEs were considered to be treatment-emergent (TEAEs) if they started or worsened after the start of first study drug administration until 30 days after regorafenib treatment discontinuation or 100 days after the last dose of nivolumab, whatever occurred later. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to the last participant has been followed for approximately 10 months, summed up to approximately 26 months | |

| End point values | HNSCC (IO naive) | HNSCC (IO treated) | ESCC | PDAC |
|------------------------------|------------------|--------------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 30 | 20 | 30 | 20 |
| Units: Subjects | | | | |
| Any AE | 30 | 20 | 30 | 20 |
| Worst grade: Grade 1 | 1 | 0 | 2 | 0 |
| Worst grade: Grade 2 | 4 | 1 | 6 | 2 |
| Worst grade: Grade 3 | 16 | 16 | 18 | 11 |
| Worst grade: Grade 4 | 6 | 2 | 2 | 2 |
| Worst grade: Grade 5 (death) | 3 | 1 | 2 | 5 |

| End point values | Biliary Tract Cancer (BTC) | GBM/AA | | |
|------------------------------|----------------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 30 | | |
| Units: Subjects | | | | |
| Any AE | 45 | 30 | | |
| Worst grade: Grade 1 | 1 | 0 | | |
| Worst grade: Grade 2 | 9 | 8 | | |
| Worst grade: Grade 3 | 23 | 11 | | |
| Worst grade: Grade 4 | 1 | 2 | | |
| Worst grade: Grade 5 (death) | 11 | 9 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After the start of first study drug administration until 30 days after regorafenib treatment discontinuation or 100 days after the last dose of nivolumab, whatever occurred later.

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 26 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | HNSCC (IO naive) |
|-----------------------|------------------|

Reporting group description:

Participants with confirmed recurrent or metastatic HNSCC and IO naive, received regorafenib in combination with nivolumab. (treatment details refers to Description under Participant Flow section above)

| | |
|-----------------------|--------|
| Reporting group title | GBM/AA |
|-----------------------|--------|

Reporting group description:

Participants with GBM or AA received regorafenib in combination with nivolumab. (treatment details refers to Description under Participant Flow section above)

| | |
|-----------------------|------|
| Reporting group title | PDAC |
|-----------------------|------|

Reporting group description:

Participants with confirmed recurrent or metastatic PADC received regorafenib in combination with nivolumab. (treatment details refers to Description under Participant Flow section above)

| | |
|-----------------------|----------------------------|
| Reporting group title | Biliary Tract Cancer (BTC) |
|-----------------------|----------------------------|

Reporting group description:

Participants with confirmed recurrent or metastatic BTC received regorafenib in combination with nivolumab. (treatment details refers to Description under Participant Flow section above)

| | |
|-----------------------|--------------------|
| Reporting group title | HNSCC (IO treated) |
|-----------------------|--------------------|

Reporting group description:

Participants with confirmed recurrent or metastatic HNSCC and with IO treated, received regorafenib in combination with nivolumab. (treatment details refers to Description under Participant Flow section above)

| | |
|-----------------------|------|
| Reporting group title | ESCC |
|-----------------------|------|

Reporting group description:

Participants with confirmed recurrent or metastatic ESCC received regorafenib in combination with nivolumab. (treatment details refers to Description under Participant Flow section above)

| Serious adverse events | HNSCC (IO naive) | GBM/AA | PDAC |
|---|------------------|------------------|------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 22 / 30 (73.33%) | 13 / 30 (43.33%) | 13 / 20 (65.00%) |
| number of deaths (all causes) | 22 | 27 | 17 |
| number of deaths resulting from adverse events | 3 | 9 | 5 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Bladder cancer | | | |

| | | | |
|--|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Pharyngeal cancer | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Bile duct stent insertion | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 9 / 30 (30.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 10 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 9 | 0 / 1 |
| Performance status decreased | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |

| | | | |
|---|----------------|----------------|----------------|
| Pyrexia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Face oedema | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (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 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemophagocytic lymphohistiocytosis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung disorder | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngeal stenosis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (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 |
| Obstructive airways disorder | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (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 |
| Product issues | | | |
| Device occlusion | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device deposit issue | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 30 (3.33%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 30 (3.33%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver function test increased | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 4 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Skull fracture | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Myocardial infarction | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Coma | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 0 / 20 (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 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 0 / 20 (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 |
| Hemiplegia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 0 / 20 (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 |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 0 / 20 (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 |
| Vasogenic cerebral oedema | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Colitis ischaemic | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (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 |
| Ileus | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysphagia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 0 / 20 (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 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (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 |
| Pneumoperitoneum | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (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 |
| Diverticular perforation | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral cavity fistula | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatitis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic failure | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (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 |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune hepatitis | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bile duct stenosis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 2 / 20 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary obstruction | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |

| | | | |
|---|-----------------|----------------|----------------|
| Hypopituitarism | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Crystal arthropathy | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (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 |
| Osteitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 30 (3.33%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| 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 respiratory tract infection | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral infection | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal abscess | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (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 |
| Biliary tract infection | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Medical device site infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (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 |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malnutrition | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (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 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Biliary Tract Cancer (BTC) | HNSCC (IO treated) | ESCC |
|---|----------------------------|--------------------|------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 28 / 45 (62.22%) | 15 / 20 (75.00%) | 19 / 30 (63.33%) |
| number of deaths (all causes) | 36 | 17 | 20 |
| number of deaths resulting from adverse events | 11 | 1 | 2 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Bladder cancer | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (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 |
| Pharyngeal cancer | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Bile duct stent insertion | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 7 / 45 (15.56%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 7 | 0 / 1 | 0 / 0 |
| Performance status decreased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Face oedema | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactic reaction | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemophagocytic lymphohistiocytosis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 2 / 30 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung disorder | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (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 |
| Laryngeal stenosis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive airways disorder | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |
| Device occlusion | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (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 |
| Device deposit issue | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (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 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Skull fracture | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Coma | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hemiplegia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (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 | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vasogenic cerebral oedema | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Colitis ischaemic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 5 / 5 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (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 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine perforation | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (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 |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (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 |
| Pneumoperitoneum | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticular perforation | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (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 |
| Oral cavity fistula | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Hepatitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic function abnormal | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic failure | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (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 |
| Cholangitis | | | |
| subjects affected / exposed | 5 / 45 (11.11%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune hepatitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bile duct stenosis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (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 |
| Biliary obstruction | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (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 |
| Jaundice | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (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 |
| Renal and urinary disorders | | | |
| Ureterolithiasis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Hypopituitarism | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Crystal arthropathy | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteitis | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 4 / 20 (20.00%) | 4 / 30 (13.33%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 7 | 2 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Septic shock | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (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 |
| Urinary tract infection enterococcal | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oral infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal abscess | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary tract infection | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Medical device site infection | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (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 |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | HNSCC (IO naive) | GBM/AA | PDAC |
|---|-------------------|------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 30 / 30 (100.00%) | 29 / 30 (96.67%) | 20 / 20 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Peritumoural oedema | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 30 (3.33%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | 8 / 30 (26.67%) | 6 / 20 (30.00%) |
| occurrences (all) | 7 | 16 | 13 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Haemorrhage | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Thrombophlebitis | | | |

| | | | |
|--|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Jugular vein thrombosis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | 5 / 30 (16.67%) | 8 / 20 (40.00%) |
| occurrences (all) | 5 | 10 | 18 |
| Asthenia | | | |
| subjects affected / exposed | 10 / 30 (33.33%) | 10 / 30 (33.33%) | 4 / 20 (20.00%) |
| occurrences (all) | 17 | 14 | 6 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mucosal inflammation | | | |

| | | | |
|---|----------------------|----------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 4 / 30 (13.33%) 9 | 0 / 30 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 1 / 30 (3.33%) 1 | 2 / 20 (10.00%) 2 |
| Pain subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 2 | 1 / 30 (3.33%) 2 | 0 / 20 (0.00%) 0 |
| Pyrexia subjects affected / exposed occurrences (all) | 6 / 30 (20.00%) 6 | 5 / 30 (16.67%) 6 | 7 / 20 (35.00%) 14 |
| Immune system disorders Haemophagocytic lymphohistiocytosis subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Reproductive system and breast disorders Cervix haemorrhage uterine subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Pelvic pain subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Respiratory, thoracic and mediastinal disorders Aspiration subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 3 | 0 / 30 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Alveolitis subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Dysphonia subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 3 / 30 (10.00%) 4 | 3 / 20 (15.00%) 3 |
| Cough subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 3 / 30 (10.00%) 4 | 2 / 20 (10.00%) 3 |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 7 | 0 | 1 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 1 | 0 | 2 |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rales | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 30 (6.67%) | 2 / 20 (10.00%) |
| occurrences (all) | 0 | 2 | 2 |
| Psychiatric disorders | | | |
| Insomnia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 30 (3.33%) | 3 / 30 (10.00%) | 3 / 20 (15.00%) |
| occurrences (all) | 1 | 3 | 3 |
| Depression | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 30 (6.67%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Confusional state | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 4 / 30 (13.33%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Investigations | | | |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 7 / 30 (23.33%) | 3 / 30 (10.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 14 | 12 | 5 |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 4 / 30 (13.33%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | 4 / 30 (13.33%) | 1 / 20 (5.00%) |
| occurrences (all) | 10 | 12 | 2 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 6 / 30 (20.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 11 | 0 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 30 (3.33%) | 0 / 20 (0.00%) |
| occurrences (all) | 6 | 1 | 0 |
| Heart rate increased | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 6 / 30 (20.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 13 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 12 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Neutrophil count increased | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 3 / 30 (10.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 4 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 6 / 30 (20.00%) | 1 / 30 (3.33%) | 2 / 20 (10.00%) |
| occurrences (all) | 11 | 2 | 3 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 3 / 30 (10.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 4 | 1 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count increased | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| General physical condition abnormal | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|----------------|----------------|----------------|
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Subcutaneous haematoma | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound dehiscence | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound secretion | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stoma site pain | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Congenital, familial and genetic disorders | | | |
| Hypertrophic cardiomyopathy | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |

| | | | |
|-----------------------------|----------------|-----------------|-----------------|
| Nervous system disorders | | | |
| Hyperaesthesia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hemianopia homonymous | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 6 / 30 (20.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 2 | 13 | 2 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 3 / 30 (10.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 3 / 30 (10.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Apraxia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Aphasia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 3 / 30 (10.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Neuropathy peripheral | | | |

| | | | |
|--------------------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 3 / 30 (10.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Brain oedema | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 30 (6.67%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Speech disorder | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 2 / 30 (6.67%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 3 | 1 |
| Seizure | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 5 / 30 (16.67%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 5 | 1 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 10 / 30 (33.33%) | 2 / 30 (6.67%) | 6 / 20 (30.00%) |
| occurrences (all) | 24 | 3 | 16 |
| Eosinophilia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Neutrophilia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 30 (3.33%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 2 | 1 |

| | | | |
|--|---------------------|----------------------|-----------------------|
| Thrombocytopenia subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 4 | 5 / 30 (16.67%) 9 | 3 / 20 (15.00%) 6 |
| Lymphopenia subjects affected / exposed occurrences (all) | 2 / 30 (6.67%) 3 | 2 / 30 (6.67%) 2 | 0 / 20 (0.00%) 0 |
| Ear and labyrinth disorders Tympanic membrane perforation subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Eye disorders Cataract subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Gastrointestinal disorders Aptyalism subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Abdominal distension subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 4 / 30 (13.33%) 4 | 7 / 20 (35.00%) 13 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 1 / 30 (3.33%) 1 | 2 / 20 (10.00%) 3 |
| Aphthous ulcer subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 2 / 30 (6.67%) 3 | 0 / 20 (0.00%) 0 |
| Ascites subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 3 / 20 (15.00%) 6 |
| Cheilitis subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Constipation | | | |

| | | | |
|----------------------------------|-----------------|------------------|-----------------|
| subjects affected / exposed | 7 / 30 (23.33%) | 11 / 30 (36.67%) | 7 / 20 (35.00%) |
| occurrences (all) | 8 | 15 | 9 |
| Diarrhoea | | | |
| subjects affected / exposed | 7 / 30 (23.33%) | 6 / 30 (20.00%) | 3 / 20 (15.00%) |
| occurrences (all) | 10 | 11 | 5 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 30 (6.67%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Dysphagia | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 4 | 2 | 0 |
| Oral discomfort | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 2 | 0 | 2 |
| Glossitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | 4 / 30 (13.33%) | 7 / 20 (35.00%) |
| occurrences (all) | 3 | 4 | 10 |
| Odynophagia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Eructation | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Oral pain | | | |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Periodontal disease | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | 1 / 30 (3.33%) | 1 / 20 (5.00%) |
| occurrences (all) | 16 | 1 | 4 |
| Toothache | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 5 / 20 (25.00%) |
| occurrences (all) | 2 | 0 | 8 |
| Subileus | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Oral cavity fistula | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Anal inflammation | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Cholestasis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 5 / 30 (16.67%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 9 | 3 |
| Jaundice | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Hepatic cytolysis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 2 | 0 | 1 |
| Bile duct stenosis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | 0 / 30 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 3 | 0 | 2 |
| Erythema | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 8 / 30 (26.67%) | 8 / 30 (26.67%) | 5 / 20 (25.00%) |
| occurrences (all) | 11 | 18 | 16 |
| Skin toxicity | | | |

| | | | |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Palmoplantar keratoderma | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Pruritus | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 2 | 0 | 2 |
| Psoriasis | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Purpura | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 6 / 30 (20.00%) | 5 / 30 (16.67%) | 8 / 20 (40.00%) |
| occurrences (all) | 7 | 8 | 14 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Skin exfoliation | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scar pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 5 | 4 | 0 |

| | | | |
|--|----------------------|----------------------|----------------------|
| Hydronephrosis subjects affected / exposed occurrences (all) | 1 / 30 (3.33%) 1 | 0 / 30 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Haematuria subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Glycosuria subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 1 / 20 (5.00%) 1 |
| Urinary incontinence subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 2 / 30 (6.67%) 2 | 0 / 20 (0.00%) 0 |
| Endocrine disorders | | | |
| Hyperthyroidism subjects affected / exposed occurrences (all) | 5 / 30 (16.67%) 6 | 1 / 30 (3.33%) 1 | 1 / 20 (5.00%) 1 |
| Hypopituitarism subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 1 / 20 (5.00%) 2 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 6 | 3 / 30 (10.00%) 3 | 3 / 20 (15.00%) 3 |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 1 / 30 (3.33%) 1 | 2 / 20 (10.00%) 3 |
| Neck pain subjects affected / exposed occurrences (all) | 3 / 30 (10.00%) 3 | 0 / 30 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Myalgia subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 1 / 30 (3.33%) 1 | 1 / 20 (5.00%) 1 |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 0 / 30 (0.00%) 0 | 0 / 30 (0.00%) 0 | 0 / 20 (0.00%) 0 |
| Muscular weakness | | | |

| | | | |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 3 / 30 (10.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all) | 1 | 0 | 4 |
| Back pain | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 30 (6.67%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 2 | 1 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 3 / 30 (10.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 3 | 1 |
| Amyotrophy | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle atrophy | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Sarcopenia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular device infection | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |

| | | | |
|------------------------------------|-----------------|----------------|-----------------|
| Paronychia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 8 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 1 / 30 (3.33%) | 0 / 20 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 1 / 30 (3.33%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Acinetobacter bacteraemia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Influenza | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 0 / 30 (0.00%) | 3 / 20 (15.00%) |
| occurrences (all) | 1 | 0 | 6 |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Hyperglycaemia | | | |

| | | | |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 6 / 30 (20.00%) | 3 / 20 (15.00%) |
| occurrences (all) | 0 | 10 | 3 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 2 / 30 (6.67%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | 1 / 30 (3.33%) | 5 / 20 (25.00%) |
| occurrences (all) | 6 | 1 | 8 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | 1 / 30 (3.33%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Decreased appetite | | | |
| subjects affected / exposed | 8 / 30 (26.67%) | 6 / 30 (20.00%) | 7 / 20 (35.00%) |
| occurrences (all) | 8 | 10 | 10 |
| Hyponatraemia | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | 2 / 30 (6.67%) | 1 / 20 (5.00%) |
| occurrences (all) | 3 | 3 | 1 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | 1 / 30 (3.33%) | 0 / 20 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Refeeding syndrome | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Cell death | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malnutrition | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 4 / 30 (13.33%) | 1 / 30 (3.33%) | 1 / 20 (5.00%) |
| occurrences (all) | 9 | 3 | 1 |
| Type 2 diabetes mellitus | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Steroid diabetes | | | |
| subjects affected / exposed | 0 / 30 (0.00%) | 0 / 30 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Biliary Tract Cancer (BTC) | HNSCC (IO treated) | ESCC |
|---|----------------------------|--------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 45 / 45 (100.00%) | 20 / 20 (100.00%) | 30 / 30 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Peritumoural oedema | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Tumour pain | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 3 / 20 (15.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 2 | 10 | 1 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 2 / 20 (10.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 11 / 45 (24.44%) | 7 / 20 (35.00%) | 4 / 30 (13.33%) |
| occurrences (all) | 25 | 12 | 7 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhage | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombophlebitis | | | |

| | | | |
|--|------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Jugular vein thrombosis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 19 / 45 (42.22%) | 7 / 20 (35.00%) | 9 / 30 (30.00%) |
| occurrences (all) | 43 | 16 | 19 |
| Asthenia | | | |
| subjects affected / exposed | 12 / 45 (26.67%) | 2 / 20 (10.00%) | 7 / 30 (23.33%) |
| occurrences (all) | 36 | 6 | 24 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Chest pain | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 20 (0.00%) | 4 / 30 (13.33%) |
| occurrences (all) | 2 | 0 | 5 |
| Chills | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 1 | 0 | 4 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 | 1 |
| Mucosal inflammation | | | |

| | | | |
|---|------------------------|-----------------------|------------------------|
| subjects affected / exposed occurrences (all) | 5 / 45 (11.11%) 8 | 1 / 20 (5.00%) 2 | 4 / 30 (13.33%) 14 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 4 / 45 (8.89%) 6 | 1 / 20 (5.00%) 1 | 1 / 30 (3.33%) 2 |
| Pain subjects affected / exposed occurrences (all) | 1 / 45 (2.22%) 4 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Pyrexia subjects affected / exposed occurrences (all) | 17 / 45 (37.78%) 43 | 6 / 20 (30.00%) 10 | 12 / 30 (40.00%) 20 |
| Immune system disorders Haemophagocytic lymphohistiocytosis subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Reproductive system and breast disorders Cervix haemorrhage uterine subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Pelvic pain subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Aspiration subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Alveolitis subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Dysphonia subjects affected / exposed occurrences (all) | 9 / 45 (20.00%) 9 | 2 / 20 (10.00%) 2 | 5 / 30 (16.67%) 6 |
| Cough subjects affected / exposed occurrences (all) | 4 / 45 (8.89%) 4 | 2 / 20 (10.00%) 2 | 4 / 30 (13.33%) 5 |

| | | | |
|-----------------------------|----------------|-----------------|-----------------|
| Dyspnoea | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | 2 / 20 (10.00%) | 5 / 30 (16.67%) |
| occurrences (all) | 6 | 2 | 7 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 1 / 20 (5.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 1 | 1 | 3 |
| Epistaxis | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 | 1 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 5 / 30 (16.67%) |
| occurrences (all) | 0 | 0 | 10 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rales | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 1 | 0 | 1 |
| Psychiatric disorders | | | |
| Insomnia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 7 / 45 (15.56%) | 4 / 20 (20.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 8 | 4 | 2 |
| Depression | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 1 | 0 | 1 |
| Investigations | | | |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 1 / 20 (5.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 4 | 1 | 1 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | 2 / 20 (10.00%) | 4 / 30 (13.33%) |
| occurrences (all) | 7 | 8 | 10 |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 0 | 0 | 4 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 5 / 45 (11.11%) | 2 / 20 (10.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 9 | 6 | 6 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 6 / 45 (13.33%) | 2 / 20 (10.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 10 | 2 | 1 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 2 / 20 (10.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Heart rate increased | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 1 / 20 (5.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 4 | 1 | 6 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 3 | 0 | 1 |
| Neutrophil count increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 2 / 20 (10.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 5 | 2 | 5 |
| Weight decreased | | | |
| subjects affected / exposed | 5 / 45 (11.11%) | 3 / 20 (15.00%) | 6 / 30 (20.00%) |
| occurrences (all) | 6 | 3 | 7 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Platelet count increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General physical condition abnormal | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

| | | | |
|--|----------------|-----------------|----------------|
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 | 1 |
| Subcutaneous haematoma | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Wound dehiscence | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Wound secretion | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Stoma site pain | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Congenital, familial and genetic disorders | | | |
| Hypertrophic cardiomyopathy | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 3 | 0 | 2 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 3 / 20 (15.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 3 | 2 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 3 | 0 | 1 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Nervous system disorders | | | |
| Hyperaesthesia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hemiparesis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hemianopia homonymous | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 1 / 20 (5.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 3 | 1 | 2 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 5 | 0 | 2 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 1 | 0 | 2 |
| Apraxia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aphasia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Memory impairment | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neuropathy peripheral | | | |

| | | | |
|--------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Brain oedema | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Speech disorder | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 3 / 20 (15.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 1 | 0 | 2 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 7 / 45 (15.56%) | 3 / 20 (15.00%) | 5 / 30 (16.67%) |
| occurrences (all) | 8 | 7 | 12 |
| Eosinophilia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophilia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|------------------------|---------------------|----------------------|
| Thrombocytopenia subjects affected / exposed occurrences (all) | 9 / 45 (20.00%) 11 | 0 / 20 (0.00%) 0 | 1 / 30 (3.33%) 1 |
| Lymphopenia subjects affected / exposed occurrences (all) | 1 / 45 (2.22%) 1 | 0 / 20 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Ear and labyrinth disorders Tympanic membrane perforation subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Eye disorders Cataract subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Gastrointestinal disorders Aptyalism subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Abdominal distension subjects affected / exposed occurrences (all) | 2 / 45 (4.44%) 2 | 1 / 20 (5.00%) 1 | 2 / 30 (6.67%) 2 |
| Abdominal pain subjects affected / exposed occurrences (all) | 11 / 45 (24.44%) 16 | 1 / 20 (5.00%) 2 | 4 / 30 (13.33%) 5 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 8 / 45 (17.78%) 12 | 1 / 20 (5.00%) 1 | 5 / 30 (16.67%) 5 |
| Aphthous ulcer subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Ascites subjects affected / exposed occurrences (all) | 1 / 45 (2.22%) 1 | 0 / 20 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Cheilitis subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Constipation | | | |

| | | | |
|----------------------------------|------------------|-----------------|------------------|
| subjects affected / exposed | 15 / 45 (33.33%) | 8 / 20 (40.00%) | 7 / 30 (23.33%) |
| occurrences (all) | 20 | 10 | 10 |
| Diarrhoea | | | |
| subjects affected / exposed | 17 / 45 (37.78%) | 3 / 20 (15.00%) | 11 / 30 (36.67%) |
| occurrences (all) | 31 | 6 | 25 |
| Dry mouth | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 1 / 20 (5.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 5 | 1 | 2 |
| Dysphagia | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Oral discomfort | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 4 / 30 (13.33%) |
| occurrences (all) | 2 | 0 | 4 |
| Glossitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nausea | | | |
| subjects affected / exposed | 14 / 45 (31.11%) | 2 / 20 (10.00%) | 5 / 30 (16.67%) |
| occurrences (all) | 19 | 2 | 6 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Eructation | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral pain | | | |

| | | | |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 0 | 7 |
| Periodontal disease | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 3 / 20 (15.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 4 | 7 | 8 |
| Toothache | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Vomiting | | | |
| subjects affected / exposed | 8 / 45 (17.78%) | 1 / 20 (5.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 9 | 1 | 3 |
| Subileus | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral cavity fistula | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anal inflammation | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hepatobiliary disorders | | | |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 8 | 0 | 0 |
| Cholestasis | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 3 | 0 | 1 |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 0 | 4 |

| | | | |
|---|------------------|-----------------|------------------|
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 9 | 0 | 0 |
| Jaundice | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatic cytolysis | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 2 | 0 | 2 |
| Bile duct stenosis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 3 / 20 (15.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 2 | 3 | 1 |
| Decubitus ulcer | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 1 / 20 (5.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 2 | 1 | 1 |
| Dry skin | | | |
| subjects affected / exposed | 6 / 45 (13.33%) | 1 / 20 (5.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 6 | 1 | 3 |
| Erythema | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 1 / 20 (5.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 2 | 1 | 1 |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 15 / 45 (33.33%) | 9 / 20 (45.00%) | 22 / 30 (73.33%) |
| occurrences (all) | 37 | 28 | 45 |
| Skin toxicity | | | |

| | | | |
|--|------------------------|----------------------|------------------------|
| subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Palmoplantar keratoderma subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 5 / 45 (11.11%) 5 | 2 / 20 (10.00%) 3 | 3 / 30 (10.00%) 4 |
| Psoriasis subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Purpura subjects affected / exposed occurrences (all) | 1 / 45 (2.22%) 1 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Rash subjects affected / exposed occurrences (all) | 10 / 45 (22.22%) 22 | 2 / 20 (10.00%) 2 | 14 / 30 (46.67%) 23 |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 5 / 45 (11.11%) 8 | 3 / 20 (15.00%) 3 | 0 / 30 (0.00%) 0 |
| Skin exfoliation subjects affected / exposed occurrences (all) | 1 / 45 (2.22%) 2 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Scar pain subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) | 3 / 45 (6.67%) 6 | 0 / 20 (0.00%) 0 | 1 / 30 (3.33%) 1 |
| Urinary retention subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Proteinuria subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 4 / 20 (20.00%) 4 | 1 / 30 (3.33%) 2 |

| | | | |
|--|----------------------|----------------------|-----------------------|
| Hydronephrosis subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Haematuria subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 20 (0.00%) 0 | 2 / 30 (6.67%) 2 |
| Glycosuria subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Urinary incontinence subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 0 / 20 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Endocrine disorders | | | |
| Hyperthyroidism subjects affected / exposed occurrences (all) | 6 / 45 (13.33%) 6 | 1 / 20 (5.00%) 1 | 2 / 30 (6.67%) 2 |
| Hypopituitarism subjects affected / exposed occurrences (all) | 3 / 45 (6.67%) 6 | 0 / 20 (0.00%) 0 | 0 / 30 (0.00%) 0 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 5 / 45 (11.11%) 7 | 5 / 20 (25.00%) 6 | 8 / 30 (26.67%) 10 |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 3 / 45 (6.67%) 6 | 0 / 20 (0.00%) 0 | 1 / 30 (3.33%) 2 |
| Neck pain subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 4 / 20 (20.00%) 4 | 1 / 30 (3.33%) 1 |
| Myalgia subjects affected / exposed occurrences (all) | 5 / 45 (11.11%) 8 | 1 / 20 (5.00%) 1 | 4 / 30 (13.33%) 4 |
| Musculoskeletal pain subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | 1 / 20 (5.00%) 1 | 0 / 30 (0.00%) 0 |
| Muscular weakness | | | |

| | | | |
|-----------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 7 / 45 (15.56%) | 2 / 20 (10.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 10 | 2 | 2 |
| Back pain | | | |
| subjects affected / exposed | 10 / 45 (22.22%) | 0 / 20 (0.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 12 | 0 | 4 |
| Arthritis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Arthralgia | | | |
| subjects affected / exposed | 6 / 45 (13.33%) | 1 / 20 (5.00%) | 5 / 30 (16.67%) |
| occurrences (all) | 8 | 1 | 6 |
| Amyotrophy | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle atrophy | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sarcopenia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vascular device infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|------------------------------------|----------------|-----------------|-----------------|
| Paronychia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 1 | 2 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | 2 / 20 (10.00%) | 4 / 30 (13.33%) |
| occurrences (all) | 3 | 2 | 8 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 1 / 20 (5.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 4 | 1 | 2 |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acinetobacter bacteraemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| COVID-19 | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | 0 / 20 (0.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 4 | 0 | 4 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 0 | 0 | 4 |
| Hyperglycaemia | | | |

| | | | |
|-----------------------------|------------------|-----------------|------------------|
| subjects affected / exposed | 1 / 45 (2.22%) | 0 / 20 (0.00%) | 2 / 30 (6.67%) |
| occurrences (all) | 2 | 0 | 2 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 5 / 45 (11.11%) | 0 / 20 (0.00%) | 4 / 30 (13.33%) |
| occurrences (all) | 10 | 0 | 9 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | 1 / 20 (5.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 4 | 2 | 2 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 14 / 45 (31.11%) | 9 / 20 (45.00%) | 11 / 30 (36.67%) |
| occurrences (all) | 25 | 16 | 26 |
| Hyponatraemia | | | |
| subjects affected / exposed | 4 / 45 (8.89%) | 0 / 20 (0.00%) | 3 / 30 (10.00%) |
| occurrences (all) | 8 | 0 | 6 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 5 / 45 (11.11%) | 1 / 20 (5.00%) | 1 / 30 (3.33%) |
| occurrences (all) | 5 | 1 | 1 |
| Refeeding syndrome | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cell death | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Malnutrition | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 5 / 45 (11.11%) | 1 / 20 (5.00%) | 4 / 30 (13.33%) |
| occurrences (all) | 6 | 1 | 4 |
| Type 2 diabetes mellitus | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 45 (0.00%) | 0 / 20 (0.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Steroid diabetes | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | 1 / 20 (5.00%) | 0 / 30 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 21 January 2021 | Global amendment 01 introduced the following changes: The Schedule of Activities were updated to more clearly define the timing of the CT/MRIs and the collection of AEs during follow-up. Additional wording on trial stop was added. Additional inclusion criteria for Stage 2 participants were added to clarify previous therapies allowed. Updated guidance regarding male contraception based on the updated nivolumab Investigator's Brochure. Dose modification tables for regorafenib were updated. Nivolumab toxicity management guidelines updated to reflect incorporation of CTCAE v.5.0, as well as changes consistent with updated nivolumab immune-mediated AE management algorithms. Recommended dose modification for nivolumab updated according to the newest management algorithms for studies, under CTCAE v5.0. AE management algorithms were updated. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported