



Clinical trial results:

An open-label first-in-human phase 1/2a study to evaluate safety, feasibility and efficacy of multiple dosing with individualised VB10.NEO or VB10.NEO and bempegaldesleukin (NKTR-214) immunotherapy in patients with locally advanced or metastatic melanoma, NSCLC, clear renal cell carcinoma, urothelial cancer or squamous cell carcinoma of head and neck, who did not reach complete responses with current standard of care immune checkpoint blockade.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2017-002474-39 |
| Trial protocol | DE |
| Global end of trial date | 30 January 2023 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 |
| This version publication date | 15 February 2024 |
| First version publication date | 15 February 2024 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | VB N-01 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03548467 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Nykode Therapeutics ASA |
| Sponsor organisation address | Gaustadalléen 21, Oslo, Norway, |
| Public contact | Medical Expert, Nykode Therapeutics ASA, +47 22958193, storhaug@nykode.com |
| Scientific contact | Medical Expert, Nykode Therapeutics ASA, +47 22958193, storhaug@nykode.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 | 30 January 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 January 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 30 January 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To assess the safety/tolerability of multiple doses of 3 mg VB10.NEO immunotherapy and of multiple doses of 3 mg VB10.NEO immunotherapy in combination with 0.006 mg/kg bempegaldesleukin.

To determine the feasibility of VB10.NEO (overall process feasibility from biopsy, sequencing, neoepitope selection and vaccine manufacturing).

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki, adopted by the 18th World Medical Association (WMA) General Assembly, Helsinki, Finland, June 1964, and subsequent amendments and International Council for Harmonisation (ICH) Guideline for Good Clinical Practice E6 (R2) (European Medicines Agency (EMA)/Committee for Medicinal Products for Human Use CHMP)/ICH/135/1995), including archiving of essential documents and the EU Clinical Trial Directive (CTD)2001/20/EC.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 01 December 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Germany: 41 |
| Worldwide total number of subjects | 41 |
| EEA total number of subjects | 41 |

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) | 25 |
| From 65 to 84 years | 16 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 9 study centres in Germany.

Pre-assignment

Screening details:

Participants were assigned to VB10.NEO treatment in 1 of 5 different arms depending on tumor type.

Arm 1: melanoma; Arm 2: non-small cell lung cancer; Arm 3: clear-cell renal carcinoma; Arm 4: urothelial cancer; Arm 5: squamous cell carcinoma of the head and neck. Arm 5 was further divided into 5A and 5B, where Arm 5B also received NKTR-214.

Period 1

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

Arms

| | |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes |
| Arm title | Arm #1 |

Arm description:

Melanoma

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | VB10.NEO |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

VB10.NEO, 3 mg/dose with 3 vaccinations Q3W during the induction period, followed by maintenance period with vaccinations Q4W for up to 1 year from first immunisation (total of 14 vaccinations).

| | |
|------------------|--------|
| Arm title | Arm #2 |
|------------------|--------|

Arm description:

NSCLC

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | VB10.NEO |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

VB10.NEO, 3 mg/dose with 3 vaccinations Q3W during the induction period, followed by maintenance period with vaccinations Q4W for up to 1 year from first immunisation (total of 14 vaccinations).

| | |
|------------------|--------|
| Arm title | Arm #3 |
|------------------|--------|

Arm description:

RCC

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

| | |
|--|-------------------|
| Investigational medicinal product name | VB10.NEO |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

VB10.NEO, 3 mg/dose with 3 vaccinations Q3W during the induction period, followed by maintenance period with vaccinations Q4W for up to 1 year from first immunisation (total of 14 vaccinations).

| | |
|------------------|--------|
| Arm title | Arm #4 |
|------------------|--------|

Arm description:

Urothelial

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | VB10.NEO |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

VB10.NEO, 3 mg/dose with 3 vaccinations Q3W during the induction period, followed by maintenance period with vaccinations Q4W for up to 1 year from first immunisation (total of 14 vaccinations).

| | |
|------------------|---------|
| Arm title | Arm #5A |
|------------------|---------|

Arm description:

SCCHN

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | VB10.NEO |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

VB10.NEO, 3 mg/dose with 3 vaccinations Q3W during the induction period, followed by maintenance period with vaccinations Q4W for up to 1 year from first immunisation (total of 14 vaccinations).

| | |
|------------------|---------|
| Arm title | Arm #5B |
|------------------|---------|

Arm description:

SCCHN VB10.NEO and NKTR-214

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | VB10.NEO |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

VB10.NEO, 3 mg/dose with 3 vaccinations Q3W during the induction period, followed by maintenance period with vaccinations Q4W for up to 1 year from first immunisation (total of 14 vaccinations).

| | |
|--|-------------------|
| Investigational medicinal product name | NKTR-214 |
| Investigational medicinal product code | |
| Other name | Bempegaldesleukin |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

NKTR-214 (Bempegaldesleukin) 0.006 mg/kg was administered IV starting from Week 11 (Visit 8A or at any dosing visit up to Week 34 [Visit 14]) and up to Week 50 (up to 11 doses). The first 2 doses were in a Q3W interval and the following doses in Q4W intervals.

| Number of subjects in period 1 | Arm #1 | Arm #2 | Arm #3 |
|---------------------------------------|--------|--------|--------|
| Started | 8 | 5 | 10 |
| Completed | 3 | 2 | 7 |
| Not completed | 5 | 3 | 3 |
| Adverse event, serious fatal | 1 | 1 | - |
| Consent withdrawn by subject | - | - | - |
| Disease progression | 1 | 1 | 2 |
| Adverse event, non-fatal | - | 1 | - |
| Other | 2 | - | 1 |
| Protocol deviation | 1 | - | - |

| Number of subjects in period 1 | Arm #4 | Arm #5A | Arm #5B |
|---------------------------------------|--------|---------|---------|
| Started | 4 | 8 | 6 |
| Completed | 2 | 2 | 3 |
| Not completed | 2 | 6 | 3 |
| Adverse event, serious fatal | 1 | 1 | - |
| Consent withdrawn by subject | - | 2 | - |
| Disease progression | 1 | 2 | 2 |
| Adverse event, non-fatal | - | 1 | - |
| Other | - | - | 1 |
| Protocol deviation | - | - | - |

Baseline characteristics

Reporting groups

| | |
|------------------------------|---------|
| Reporting group title | Arm #1 |
| Reporting group description: | |
| Melanoma | |
| Reporting group title | Arm #2 |
| Reporting group description: | |
| NSCLC | |
| Reporting group title | Arm #3 |
| Reporting group description: | |
| RCC | |
| Reporting group title | Arm #4 |
| Reporting group description: | |
| Urothelial | |
| Reporting group title | Arm #5A |
| Reporting group description: | |
| SCCHN | |
| Reporting group title | Arm #5B |
| Reporting group description: | |
| SCCHN VB10.NEO and NKTR-214 | |

| Reporting group values | Arm #1 | Arm #2 | Arm #3 |
|------------------------|--------|--------|--------|
| Number of subjects | 8 | 5 | 10 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 5 | 4 | 7 |
| From 65-84 years | 3 | 1 | 3 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 5 | 3 | 3 |
| Male | 3 | 2 | 7 |

| Reporting group values | Arm #4 | Arm #5A | Arm #5B |
|------------------------|--------|---------|---------|
| Number of subjects | 4 | 8 | 6 |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 1 | 5 | 3 |
| From 65-84 years | 3 | 3 | 3 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 3 | 2 |
| Male | 4 | 5 | 4 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 41 | | |

| | | | |
|----------------------|----|--|--|
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 25 | | |
| From 65-84 years | 16 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 16 | | |
| Male | 25 | | |

Subject analysis sets

| | |
|---|---------------------|
| Subject analysis set title | Safety analysis set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All subjects receiving at least one dose VB10.NEO | |

| Reporting group values | Safety analysis set | | |
|------------------------|---------------------|--|--|
| Number of subjects | 41 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 25 | | |
| From 65-84 years | 16 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 16 | | |
| Male | 25 | | |

End points

End points reporting groups

| | |
|--|---------------------|
| Reporting group title | Arm #1 |
| Reporting group description: Melanoma | |
| Reporting group title | Arm #2 |
| Reporting group description: NSCLC | |
| Reporting group title | Arm #3 |
| Reporting group description: RCC | |
| Reporting group title | Arm #4 |
| Reporting group description: Urothelial | |
| Reporting group title | Arm #5A |
| Reporting group description: SCCHN | |
| Reporting group title | Arm #5B |
| Reporting group description: SCCHN VB10.NEO and NKTR-214 | |
| Subject analysis set title | Safety analysis set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All subjects receiving at least one dose VB10.NEO | |

Primary: Number of patients with treatment emergent adverse events

| | |
|---|--|
| End point title | Number of patients with treatment emergent adverse events ^[1] |
| End point description: A TEAE was defined as any AE that had an onset on or after the date of first vaccination or any preexisting condition that had worsened on or after the date of first vaccination. If it could not be determined whether the AE was treatment-emergent due to a partial onset date, it was counted as treatment-emergent. | |
| End point type | Primary |
| End point timeframe: From first VB10.NEO vaccination to 30 days after last VB10.NEO vaccination | |

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: This is a safety endpoint and no statistical analysis was performed.

| End point values | Arm #1 | Arm #2 | Arm #3 | Arm #4 |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 5 | 10 | 4 |
| Units: Patients with events | 8 | 5 | 9 | 4 |

| End point values | Arm #5A | Arm #5B | Safety analysis set | |
|------------------|---------|---------|---------------------|--|
|------------------|---------|---------|---------------------|--|

| | | | | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 8 | 6 | 41 | |
| Units: Patients with events | 8 | 6 | 40 | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with TEAEs leading to treatment discontinuation

| | |
|-----------------|---|
| End point title | Number of patients with TEAEs leading to treatment discontinuation ^[2] |
|-----------------|---|

End point description:

A TEAE leading to treatment discontinuation was defined as any TEAE where the outcome was registered as treatment discontinuation.

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

End point timeframe:

From first VB10.NEO vaccination to 30 days after last VB10.NEO vaccination

Notes:

[2] - 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: This is a safety endpoint and no statistical analysis was performed.

| End point values | Arm #1 | Arm #2 | Arm #3 | Arm #4 |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 5 | 10 | 4 |
| Units: Number of patients | 1 | 1 | 0 | 1 |

| End point values | Arm #5A | Arm #5B | Safety analysis set | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 8 | 6 | 41 | |
| Units: Number of patients | 2 | 1 | 6 | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with TEAEs ≥grade 3 according to CTCAE

| | |
|-----------------|--|
| End point title | Number of patients with TEAEs ≥grade 3 according to CTCAE ^[3] |
|-----------------|--|

End point description:

All AEs were graded 1-5 according to the CTCAE grading system.

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

End point timeframe:

From first VB10.NEO vaccination to 30 days after last VB10.NEO vaccination

Notes:

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

Justification: This is a safety endpoint and no statistical analysis was performed.

| End point values | Arm #1 | Arm #2 | Arm #3 | Arm #4 |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 5 | 10 | 4 |
| Units: Number of patients | 4 | 2 | 3 | 4 |

| End point values | Arm #5A | Arm #5B | Safety analysis set | |
|-----------------------------|-----------------|-----------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 8 | 6 | 41 | |
| Units: Number of patients | 7 | 4 | 24 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first VB10.NEO vaccination to 30 days after last VB10.NEO vaccination

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 26.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | Arm #1 |
|-----------------------|--------|

Reporting group description:

Melanoma

| | |
|-----------------------|--------|
| Reporting group title | Arm #2 |
|-----------------------|--------|

Reporting group description:

NSCLC

| | |
|-----------------------|--------|
| Reporting group title | Arm #3 |
|-----------------------|--------|

Reporting group description:

RCC

| | |
|-----------------------|--------|
| Reporting group title | Arm #4 |
|-----------------------|--------|

Reporting group description:

Urothelial

| | |
|-----------------------|---------|
| Reporting group title | Arm #5A |
|-----------------------|---------|

Reporting group description:

SCCHN

| | |
|-----------------------|---------|
| Reporting group title | Arm #5B |
|-----------------------|---------|

Reporting group description:

SCCHN VB10.NEO and NKTR-214

| | |
|-----------------------|-------|
| Reporting group title | Total |
|-----------------------|-------|

Reporting group description:

Pool of all patients

| Serious adverse events | Arm #1 | Arm #2 | Arm #3 |
|---|----------------|----------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 8 (62.50%) | 3 / 5 (60.00%) | 2 / 10 (20.00%) |
| number of deaths (all causes) | 2 | 3 | 5 |
| number of deaths resulting from adverse events | 1 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Neoplasm progression | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| 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 | | | |

| | | | |
|---|----------------|----------------|-----------------|
| Postoperative care | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (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 |
| Routine health maintenance | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Bronchostenosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (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 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune-mediated lung disease | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Ileus | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (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 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| 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 | | | |
| Biopsy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Panendoscopy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| 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 | | | |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (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 |
| Radiation skin injury | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| 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 | | | |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (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 arrest | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| 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 | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| 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 | | | |
| Pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (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 |
| Gastrointestinal disorders | | | |
| Subileus | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (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 |
| Autoimmune colitis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (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 |

| | | | |
|---|---------------|----------------|-----------------|
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholestasis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (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 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| 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 | | | |
| Osteonecrosis of jaw | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (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 |
| Abscess neck | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 | | | |

| | | | |
|---|---------------|---------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular device infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Arm #4 | Arm #5A | Arm #5B |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | 7 / 8 (87.50%) | 3 / 6 (50.00%) |
| number of deaths (all causes) | 2 | 3 | 1 |
| number of deaths resulting from adverse events | 1 | 1 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Neoplasm progression | | | |

| | | | |
|---|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Surgical and medical procedures | | | |
| Postoperative care | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Routine health maintenance | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| 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 | | | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchostenosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| 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 lung disease | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (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 |
| Ileus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Biopsy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (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 |
| Panendoscopy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radiation skin injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (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 | | | |
| Atrioventricular block complete | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (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 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (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 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (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 | | | |
| Pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| 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 | | | |
| Subileus | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (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 |

| | | | |
|---|---------------|----------------|----------------|
| Autoimmune colitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| 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 | | | |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (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 |
| Cholestasis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Osteonecrosis of jaw | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| 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 | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 8 (25.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess neck | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis bacterial | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| 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 | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (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 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular device infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|------------------|--|--|
| Serious adverse events | Total | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 23 / 41 (56.10%) | | |
| number of deaths (all causes) | 16 | | |
| number of deaths resulting from adverse events | 3 | | |

| | | | |
|---|----------------|--|--|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Neoplasm progression | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Surgical and medical procedures | | | |
| Postoperative care | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Routine health maintenance | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Bronchostenosis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune-mediated lung disease | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ileus | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Biopsy | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Panendoscopy | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Radiation skin injury | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Cardiac disorders | | | |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Pain | | | |
| subjects affected / exposed | 0 / 41 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Subileus | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Autoimmune colitis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Cholangitis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholestasis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteonecrosis of jaw | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abscess neck | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infection | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular device infection | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Arm #1 | Arm #2 | Arm #3 |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 8 (100.00%) | 5 / 5 (100.00%) | 9 / 10 (90.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Melanocytic naevus | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neoplasm progression | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Papilloma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 3 / 10 (30.00%) |
| occurrences (all) | 0 | 0 | 14 |
| Aneurysm arteriovenous | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematoma | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypotension | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Peripheral venous disease subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Surgical and medical procedures | | | |
| Tooth extraction subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Cancer surgery subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Postoperative care subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Routine health maintenance subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Fatigue subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 2 / 5 (40.00%) 2 | 4 / 10 (40.00%) 5 |
| Pyrexia subjects affected / exposed occurrences (all) | 2 / 8 (25.00%) 4 | 1 / 5 (20.00%) 1 | 1 / 10 (10.00%) 1 |
| Mucosal inflammation subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 2 / 5 (40.00%) 2 | 2 / 10 (20.00%) 2 |
| Pain subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Chills subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 3 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Condition aggravated | | | |

| | | | |
|---------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 4 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injection site haematoma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Malaise | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Adverse reaction | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Face oedema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Impaired healing | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site bruising | | | |

| | | | |
|--|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site reaction | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site swelling | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Swelling | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Swelling face | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Adverse drug reaction | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infusion site pruritus | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Breast pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Genital rash | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Pelvic pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scrotal dermatitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 3 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Cough | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 0 | 7 |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchostenosis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoxia | | | |

| | | | |
|------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Immune-mediated lung disease | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngeal inflammation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pulmonary pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhonchi | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stridor | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Throat tightness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--------------------------------------|----------------|----------------|-----------------|
| Agitation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Conversion disorder | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Delirium | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 1 / 5 (20.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 2 | 1 | 6 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 1 / 5 (20.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 4 | 1 | 1 |
| Lipase increased | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 1 / 5 (20.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 4 | 1 | 1 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 3 | 0 | 2 |
| Weight decreased | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 3 / 10 (30.00%) |
| occurrences (all) | 1 | 0 | 3 |
| Amylase increased | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 3 | 0 | 1 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 1 | 0 | 2 |
| Biopsy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood albumin decreased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood creatine increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| N-terminal prohormone brain natriuretic peptide increased | | | |

| | | | |
|--|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Panendoscopy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Protein total increased | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Facial bones fracture | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Fracture | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immunisation reaction | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Radiation skin injury | | | |

| | | | |
|---------------------------------|----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Synovial rupture | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Bundle branch block right | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Polyneuropathy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ageusia | | | |

| | | | |
|------------------------------|----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysaesthesia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial paresis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fine motor skill dysfunction | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Monoparesis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post herpetic neuralgia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |

| | | | |
|--|--------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 2 / 5 (40.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 4 | 4 | 1 |
| Lymphopenia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Eosinophilia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymph node pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Neutrophilia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Ear haemorrhage | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Eye disorders | | | |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| Cataract | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chalazion | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Entropion | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 3 / 5 (60.00%) | 3 / 10 (30.00%) |
| occurrences (all) | 2 | 3 | 3 |
| Nausea | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 1 / 5 (20.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 2 | 1 | 1 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 2 / 5 (40.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 3 | 2 | 1 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Food poisoning | | | |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Oral disorder | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Subileus | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Angular cheilitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ascites | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Autoimmune colitis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ileus | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stomatitis | | | |

| | | | |
|--|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Swollen tongue | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tongue erythema | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cholestasis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 1 | 4 |
| Erythema | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash maculo-papular | | | |

| | | | |
|--|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Eczema | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Intertrigo | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Keratosis pilaris | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Palmar-plantar erythrodysesthesia syndrome | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin disorder | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin exfoliation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|---------------------|---------------------|----------------------|
| Skin fissures subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 5 (20.00%) 1 | 0 / 10 (0.00%) 0 |
| Skin toxicity subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Renal and urinary disorders Urinary tract obstruction subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Haematuria subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Renal impairment subjects affected / exposed occurrences (all) | 2 / 8 (25.00%) 3 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Acute kidney injury subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Pollakiuria subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Endocrine disorders Adrenal insufficiency subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 2 / 10 (20.00%) 3 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Thyroid mass subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| Arthralgia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 5 (40.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 2 | 3 |
| Back pain | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 3 | 0 | 1 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Flank pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune-mediated arthritis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---------------------|---------------------|----------------------|
| Osteonecrosis of jaw subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 5 (20.00%) 2 | 0 / 10 (0.00%) 0 |
| Infections and infestations | | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 2 / 8 (25.00%) 3 | 1 / 5 (20.00%) 1 | 1 / 10 (10.00%) 1 |
| Pneumonia subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 2 / 5 (40.00%) 3 | 1 / 10 (10.00%) 1 |
| Infection subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Urinary tract infection bacterial subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Abscess neck subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Arthritis bacterial subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 1 / 10 (10.00%) 2 |
| COVID-19 subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Conjunctivitis subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Diverticulitis subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Erysipelas | | | |

| | | | |
|-----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastroenteritis bacterial | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tinea infection | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tinea pedis | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular device infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound infection | | | |

| | | | |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 5 (20.00%) 1 | 0 / 10 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 5 (20.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 5 (20.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 1 | 1 | 1 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 1 / 5 (20.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 5 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all) | 1 | 0 | 3 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 3 / 8 (37.50%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 2 / 8 (25.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Calcium deficiency | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|---------------|---------------|-----------------|
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Magnesium deficiency | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin K deficiency | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 5 (0.00%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Arm #4 | Arm #5A | Arm #5B |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | 8 / 8 (100.00%) | 6 / 6 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Melanocytic naevus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neoplasm progression | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Papilloma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour pain | | | |

| | | | |
|---|--------------------|---------------------|--------------------|
| subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 6 (0.00%) 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 3 / 8 (37.50%) | 1 / 6 (16.67%) |
| occurrences (all) | 10 | 8 | 8 |
| Aneurysm arteriovenous | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 4 |
| Peripheral venous disease | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Surgical and medical procedures | | | |
| Tooth extraction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Cancer surgery | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Postoperative care | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Routine health maintenance | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |

| | | | |
|---------------------------------------|----------------|----------------|----------------|
| Fatigue | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 4 / 8 (50.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 1 | 4 | 6 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 1 | 4 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 8 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Pain | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 1 |
| Chills | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Condition aggravated | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 3 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Injection site haematoma | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Adverse reaction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Asthenia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Face oedema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site bruising | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Injection site reaction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injection site swelling | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Swelling | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Swelling face | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Adverse drug reaction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---------------------|---------------------|---------------------|
| Infusion site pruritus subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Oedema subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 6 (0.00%) 0 |
| Reproductive system and breast disorders Breast pain subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Genital rash subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Pelvic pain subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Scrotal dermatitis subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Epistaxis subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Cough subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 6 (0.00%) 0 |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |

| | | | |
|------------------------------|----------------|----------------|----------------|
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Bronchostenosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune-mediated lung disease | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Laryngeal inflammation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 4 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhonchi | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| Stridor | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Throat tightness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Psychiatric disorders | | | |
| Sleep disorder | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Agitation | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conversion disorder | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Delirium | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 8 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 2 | 1 |
| Aspartate aminotransferase increased | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 8 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 2 | 1 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 8 (12.50%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 2 | 3 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Biopsy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood albumin decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bilirubin increased | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Panendoscopy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Protein total increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial bones fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fracture | | | |

| | | | |
|---------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Immunisation reaction | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Radiation skin injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Synovial rupture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bundle branch block right | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|------------------------------|----------------|----------------|----------------|
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 8 (12.50%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 1 |
| Polyneuropathy | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 1 |
| Syncope | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Ageusia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Dysaesthesia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Facial paresis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fine motor skill dysfunction | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Monoparesis | | | |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Post herpetic neuralgia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Lymphopenia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 1 |
| Eosinophilia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymph node pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophilia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---------------------|---------------------|---------------------|
| Thrombocytopenia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Ear haemorrhage subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Eye disorders Cataract subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Chalazion subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Entropion subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 3 / 8 (37.50%) 4 | 0 / 6 (0.00%) 0 |
| Nausea subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 2 / 8 (25.00%) 3 | 2 / 6 (33.33%) 3 |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 1 / 8 (12.50%) 1 | 2 / 6 (33.33%) 3 |
| Abdominal pain subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 8 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Dry mouth | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 2 | 1 |
| Food poisoning | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral disorder | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Subileus | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Angular cheilitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Autoimmune colitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Enteritis | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Swollen tongue | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Tongue erythema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hepatobiliary disorders | | | |
| Hepatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 8 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cholestasis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 4 / 6 (66.67%) |
| occurrences (all) | 0 | 0 | 5 |
| Erythema | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 0 | 5 |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eczema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intertrigo | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Keratosis pilaris | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---------------------|---------------------|---------------------|
| Rash erythematous subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 1 / 6 (16.67%) 3 |
| Skin disorder subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Skin exfoliation subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Skin fissures subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Skin toxicity subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 2 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 8 (12.50%) 1 | 3 / 6 (50.00%) 4 |
| Renal and urinary disorders | | | |
| Urinary tract obstruction subjects affected / exposed occurrences (all) | 2 / 4 (50.00%) 2 | 1 / 8 (12.50%) 1 | 0 / 6 (0.00%) 0 |
| Haematuria subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 1 / 8 (12.50%) 1 | 0 / 6 (0.00%) 0 |
| Renal impairment subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Acute kidney injury subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 8 (12.50%) 3 | 0 / 6 (0.00%) 0 |
| Pollakiuria subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Endocrine disorders | | | |

| | | | |
|---|----------------|----------------|----------------|
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thyroid mass | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 8 (12.50%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 2 | 1 |
| Back pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flank pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Bone pain | | | |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Immune-mediated arthritis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Osteonecrosis of jaw | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | 2 / 8 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 6 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 8 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 8 (37.50%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 3 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abscess neck | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| COVID-19 | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis bacterial | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinea infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---------------------|---------------------|---------------------|
| Tinea pedis subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Vascular device infection subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 6 (0.00%) 0 |
| Wound infection subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 1 / 8 (12.50%) 1 | 0 / 6 (0.00%) 0 |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 8 (12.50%) 1 | 0 / 6 (0.00%) 0 |
| Hypokalaemia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 8 (12.50%) 8 | 1 / 6 (16.67%) 1 |
| Dehydration subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 8 (12.50%) 1 | 1 / 6 (16.67%) 1 |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hyponatraemia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 8 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Iron deficiency | | | |

| | | | |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Calcium deficiency | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Magnesium deficiency | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 8 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Vitamin K deficiency | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 8 (12.50%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|------------------|--|--|
| Non-serious adverse events | Total | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 40 / 41 (97.56%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Melanocytic naevus | | | |

| | | | |
|---------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Neoplasm progression | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Papilloma | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Tumour pain | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 9 / 41 (21.95%) | | |
| occurrences (all) | 40 | | |
| Aneurysm arteriovenous | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 4 | | |
| Peripheral venous disease | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Surgical and medical procedures | | | |
| Tooth extraction | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Cancer surgery | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Postoperative care | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Routine health maintenance | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 14 / 41 (34.15%) | | |
| occurrences (all) | 18 | | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 41 (17.07%) | | |
| occurrences (all) | 11 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 6 / 41 (14.63%) | | |
| occurrences (all) | 6 | | |
| Pain | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 4 | | |
| Chills | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 5 | | |
| Condition aggravated | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 8 | | |
| Chest pain | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 4 | | |
| General physical health deterioration | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 3 | | |
| Injection site haematoma | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Malaise | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Adverse reaction | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Face oedema | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Generalised oedema | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Impaired healing | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Injection site bruising | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Injection site erythema | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 3 | | |
| Injection site reaction | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Injection site swelling | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Swelling | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Swelling face | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| Adverse drug reaction | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Infusion site pruritus | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Oedema | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Reproductive system and breast disorders | | | |
| Breast pain | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Genital rash | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Pelvic pain | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Scrotal dermatitis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 5 | | |
| Epistaxis | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Cough | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 7 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Bronchostenosis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Immune-mediated lung disease | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| Laryngeal inflammation | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 4 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Productive cough | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Pulmonary pain | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Rhonchi | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Stridor | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| Throat tightness | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Wheezing | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Sleep disorder | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Agitation | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |

| | | | |
|--------------------------------------|-----------------|--|--|
| Confusional state | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Conversion disorder | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Delirium | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 8 / 41 (19.51%) | | |
| occurrences (all) | 12 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 8 / 41 (19.51%) | | |
| occurrences (all) | 9 | | |
| Lipase increased | | | |
| subjects affected / exposed | 7 / 41 (17.07%) | | |
| occurrences (all) | 8 | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 6 / 41 (14.63%) | | |
| occurrences (all) | 8 | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 5 / 41 (12.20%) | | |
| occurrences (all) | 7 | | |
| Weight decreased | | | |
| subjects affected / exposed | 5 / 41 (12.20%) | | |
| occurrences (all) | 5 | | |
| Amylase increased | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 5 | | |
| Blood alkaline phosphatase increased | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 5 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 5 | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Biopsy | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Blood albumin decreased | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Blood creatine increased | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Panendoscopy | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Protein total increased | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| White blood cell count increased | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Facial bones fracture | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Fracture | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Immunisation reaction | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Radiation skin injury | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 3 | | |
| Synovial rupture | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |

| | | | |
|---------------------------------|----------------|--|--|
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| Bundle branch block right | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 4 | | |
| Polyneuropathy | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 3 | | |
| Syncope | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Ageusia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Dizziness | | | |

| | | | |
|--------------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| Dysaesthesia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Facial paresis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Fine motor skill dysfunction | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Migraine | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Monoparesis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Post herpetic neuralgia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Seizure | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 8 / 41 (19.51%) | | |
| occurrences (all) | 11 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Lymphopenia | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 5 | | |
| Eosinophilia | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 3 | | |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Lymph node pain | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| Neutrophilia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Ear haemorrhage | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Chalazion | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Entropion | | | |

| | | | |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 11 / 41 (26.83%) | | |
| occurrences (all) | 13 | | |
| Nausea | | | |
| subjects affected / exposed | 9 / 41 (21.95%) | | |
| occurrences (all) | 11 | | |
| Vomiting | | | |
| subjects affected / exposed | 9 / 41 (21.95%) | | |
| occurrences (all) | 11 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Dry mouth | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Dysphagia | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 3 | | |
| Food poisoning | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Oral disorder | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Subileus | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 3 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Toothache | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Angular cheilitis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Ascites | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Autoimmune colitis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Enteritis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Flatulence | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Ileus | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Swollen tongue | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Tongue erythema | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |

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|--|-----------------------------|-----------------|--|--|
| Hepatobiliary disorders | Hepatitis | | | |
| | subjects affected / exposed | 2 / 41 (4.88%) | | |
| | occurrences (all) | 3 | | |
| | Immune-mediated hepatitis | | | |
| | subjects affected / exposed | 2 / 41 (4.88%) | | |
| | occurrences (all) | 2 | | |
| | Cholangitis | | | |
| | subjects affected / exposed | 1 / 41 (2.44%) | | |
| Skin and subcutaneous tissue disorders | occurrences (all) | 1 | | |
| | Cholestasis | | | |
| | subjects affected / exposed | 1 / 41 (2.44%) | | |
| | occurrences (all) | 1 | | |
| | Rash | | | |
| | subjects affected / exposed | 7 / 41 (17.07%) | | |
| | occurrences (all) | 10 | | |
| | Erythema | | | |
| | subjects affected / exposed | 4 / 41 (9.76%) | | |
| | occurrences (all) | 7 | | |
| | Decubitus ulcer | | | |
| | subjects affected / exposed | 2 / 41 (4.88%) | | |
| | occurrences (all) | 2 | | |
| | Dry skin | | | |
| | subjects affected / exposed | 2 / 41 (4.88%) | | |
| | occurrences (all) | 2 | | |
| | Rash maculo-papular | | | |
| | subjects affected / exposed | 2 / 41 (4.88%) | | |
| | occurrences (all) | 2 | | |
| | Skin lesion | | | |
| | subjects affected / exposed | 2 / 41 (4.88%) | | |
| | occurrences (all) | 2 | | |
| | Alopecia | | | |
| | subjects affected / exposed | 1 / 41 (2.44%) | | |
| | occurrences (all) | 1 | | |
| | Dermatitis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Eczema | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Intertrigo | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Keratosis pilaris | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Night sweats | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| Rash erythematous | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 3 | | |
| Skin disorder | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Skin exfoliation | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Skin fissures | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Skin toxicity | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| Pruritus | | | |
| subjects affected / exposed | 5 / 41 (12.20%) | | |
| occurrences (all) | 6 | | |

| | | | |
|---|-----------------|--|--|
| Renal and urinary disorders | | | |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 3 | | |
| Haematuria | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Renal impairment | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 3 | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 3 | | |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 3 | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Thyroid mass | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 7 / 41 (17.07%) | | |
| occurrences (all) | 9 | | |
| Back pain | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 4 | | |
| Arthritis | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |

| | | | |
|-----------------------------|-----------------|--|--|
| Flank pain | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 3 | | |
| Myalgia | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Neck pain | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 3 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Pain in jaw | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Bone pain | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Immune-mediated arthritis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Osteonecrosis of jaw | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 9 / 41 (21.95%) | | |
| occurrences (all) | 15 | | |
| Pneumonia | | | |

| | | | |
|-----------------------------------|-----------------|--|--|
| subjects affected / exposed | 5 / 41 (12.20%) | | |
| occurrences (all) | 7 | | |
| Infection | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 4 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 4 | | |
| Urinary tract infection bacterial | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Abscess neck | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 2 | | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Gastroenteritis bacterial | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Gingivitis | | | |

| | | | |
|------------------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 3 | | |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Otitis media | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Tinea infection | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Tinea pedis | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Vascular device infection | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Wound infection | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 4 | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 4 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Hypokalaemia | | | |
| subjects affected / exposed | 4 / 41 (9.76%) | | |
| occurrences (all) | 11 | | |
| Dehydration | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 4 | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 4 | | |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 3 / 41 (7.32%) | | |
| occurrences (all) | 5 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Iron deficiency | | | |
| subjects affected / exposed | 2 / 41 (4.88%) | | |
| occurrences (all) | 2 | | |
| Calcium deficiency | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Magnesium deficiency | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |
| Vitamin K deficiency | | | |
| subjects affected / exposed | 1 / 41 (2.44%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 09 May 2018 | <p>The amendments in the protocol include the increase in the number of biopsies from 2 to 5 and the possibility of carrying out CT-guided biopsies, amongst others. The additional biopsies support the investigation of the mutagenic properties, the immunological activity and the clinical efficacy and make it possible to carry out the descriptive analyses outlined in the protocol.</p> <p>CT-guided biopsies replace a major surgical procedure, e.g., in the case of tumours located deep inside the body and make it possible to secure high-quality samples with sufficient tumour cell content. The investigator will decide at each visit which tumour lesions will be chosen for each patient and whether CT-guided biopsies are required.</p> |
| 13 March 2019 | <p>To account for poor clinical outcomes and short overall survival times for patients with squamous cell carcinoma of the head and neck (SCCHN), it was decided to improve the conditions of inclusion criteria of these patients to the trial. Inclusion Criteria were updated to state that SCCHN patient must be on CPI and removed the condition of "for at least 12 weeks".</p> <p>In collaboration with Nektar Therapeutics, a possible synergistic effect of VB10.NEO with bempegaldesleukin (NKTR-214) was tested in pre-clinical studies. Based on strong non-clinical data, it was decided to make NKTR-214 available to SCCHN patients in this clinical trial. As such, a new treatment arm (arm 5B) for SCCHN was created for these patients to investigate the combination of VB10.NEO with bempegaldesleukin in patients with SCCHN. To facilitate overall recruitment and increase the enrollment of SCCHN patients the number of study centers was increase from 3 to 4-8 centers. To increase the chances of patients consenting to follow-up biopsies, the total number of biopsies that can be taken per visit (all arms) has been reduced from 5 to 3. To analyse changes in the tumour microenvironment specifically related to the introduction of NKTR-214, new time points for collecting biopsies were included in arm 5B. Further, to allow inter-patient comparison, the biopsies were also included in arm 5A.</p> |
| 15 May 2019 | <p>The study protocol has been revised to include monthly checks on blood values in the 5B cohort, once treatment with bempegaldesleukin has begun.</p> |
| 05 December 2019 | <p>The decision to investigate any possible relationships between clinical responses and changes in the frequencies and repertoire of tumour-specific mutations identified in the cell-free DNA (cfDNA), with a particular focus on the neoepitopes targeted by VB10.NEO. Tumour heterogeneity may lead to different neoepitope expression patterns in different lesions in metastatic patients. Therefore, additional samples will be collected at screening and used for the neoepitope selection process to identify the optimal neoepitopes.</p> <p>Inclusion criteria for patients with melanoma have changed. This change is based on the decision to improve the conditions to enroll patients with melanoma in this trial. The waiting time from the start of CPI treatment (as standard of care) to the first dose of the IMP VB10.NEO will be shortened by dropping the requirement that CPI must have been given for at least 12 weeks at screening. Now, melanoma patients must be on CPI at screening.</p> <p>Standard of care (SoC) for the target population in the study have evolved since the initial submission of this study, and CPIs (anti PD-1 and anti PD-L1) are more commonly used as part of SoC in combination with other anti-cancer therapies. The patients in this trial will be on CPI treatment as part of their SoC. Combinations of anti-PD-1 and anti-PD-L1 with an anti-CTLA-4 agent or other anticancer therapies are allowed now if considered required at the investigator's discretion.</p> |

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| 07 April 2020 | <p>Safety update was based on clinical safety data as of 28 February 2020 and reflects the updates included in the VB10.NEO Investigator's Brochure.</p> <p>Safety update reflects the updates in the bempegaldesleukin Investigator's Brochure edition 8.0, release date 25 March 2020.</p> <p>Total potential number of patients are increased from 50 to 60 patients to allow up to 10 patients starting treatment in each of the 6 treatment arms.</p> <p>Adding information that recruitment can be halted or slowed down at times to adapt to manufacturing capacity in order to avoid over-recruitment of patients that might result in delays of vaccine supply.</p> <p>Decision to change the post vaccination observation period of 24 h after first dose to 4 h, and 2 h for subsequent vaccinations.</p> <p>Clarification on how to handle vaccination delays in case a vaccination needs to be postponed.</p> <p>Addition of follow-up visits 3 and 6 months after end of treatment including addition of blood sampling for peripheral T cell response (PBMCs) at all follow-up visits to investigate the long-term efficacy of VB10.NEO after completion or discontinuation of treatment.</p> |
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|------------------|---|---------------|
| 12 February 2020 | Investigators in the VB N-01 trial were informed about a temporary pause in the recruitment. The reason for the pause was constraints in the supply chain which lead to a backlog and an increased manufacturing time > 16 weeks. | 03 March 2020 |

Notes:

Limitations and caveats

None reported