



Clinical trial results:

A Phase 1b/2 Study of TAK-981 Plus Pembrolizumab to Evaluate the Safety, Tolerability, and Antitumor Activity of the Combination in Patients With Select Advanced or Metastatic Solid Tumors

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2020-004325-23 |
| Trial protocol | LT LV HR |
| Global end of trial date | 29 October 2024 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 |
| This version publication date | 13 November 2025 |
| First version publication date | 13 November 2025 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | TAK-981-1502 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04381650 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Takeda |
| Sponsor organisation address | 95 Hayden Ave, Lexington, MA, United States, 02421 |
| Public contact | Study Director, Takeda, TrialDisclosures@takeda.com |
| Scientific contact | Study Director, Takeda, TrialDisclosures@takeda.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 | 29 October 2024 |
| Is this the analysis of the primary completion data? | No |

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

Notes:

General information about the trial

Main objective of the trial:

The main aim of the study is to evaluate the safety, tolerability, and preliminary efficacy of TAK-981 in combination with pembrolizumab in participants who have select advanced or metastatic solid tumors.

Protection of trial subjects:

Participant signed an informed consent form (ICF) before participating in the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 17 August 2020 |
| 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 | Brazil: 35 |
| Country: Number of subjects enrolled | Japan: 18 |
| Country: Number of subjects enrolled | China: 13 |
| Country: Number of subjects enrolled | Croatia: 5 |
| Country: Number of subjects enrolled | Latvia: 3 |
| Country: Number of subjects enrolled | Lithuania: 5 |
| Country: Number of subjects enrolled | Poland: 18 |
| Country: Number of subjects enrolled | Switzerland: 6 |
| Country: Number of subjects enrolled | United States: 58 |
| Worldwide total number of subjects | 161 |
| EEA total number of subjects | 31 |

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) | 103 |
| From 65 to 84 years | 57 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at various investigative sites throughout the world from 17 August 2020 to 29 October 2024.

Pre-assignment

Screening details:

Participants with a diagnosis of advanced or metastatic solid tumors were enrolled in this study consisting of Phase 1b (Dose Escalation cohorts), and Phase 2 (Dose Expansion cohorts) periods to receive TAK-981 and pembrolizumab.

Period 1

| | |
|------------------------------|-----------------------------|
| Period 1 title | Phase 1b (Dose Escalation) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Dose Escalation: TAK-981 40 mg + Pembrolizumab |

Arm description:

Participants received TAK-981 40 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months).

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

Dosage and administration details:

Pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|--|-----------------------|
| Investigational medicinal product name | TAK-981 |
| Investigational medicinal product code | |
| Other name | Subasumstat |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

TAK-981 40 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle.

| | |
|------------------|--|
| Arm title | Dose Escalation: TAK-981 60 mg + Pembrolizumab |
|------------------|--|

Arm description:

Participants received TAK-981 60 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months).

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | TAK-981 |
| Investigational medicinal product code | |
| Other name | Subasumstat |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

| | |
|--|-----------------------|
| Dosage and administration details: | |
| TAK-981 60 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle. | |
| Investigational medicinal product name | Pembrolizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:
Pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|------------------|--|
| Arm title | Dose Escalation: TAK-981 90 mg + Pembrolizumab |
|------------------|--|

Arm description:

Participants received TAK-981 90 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months).

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | TAK-981 |
| Investigational medicinal product code | |
| Other name | Subasumstat |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

| | |
|--|-----------------------|
| Dosage and administration details: | |
| TAK-981 90 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle. | |
| Investigational medicinal product name | Pembrolizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:
Pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|------------------|---|
| Arm title | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|------------------|---|

Arm description:

Participants received TAK-981, 120 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months).

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | TAK-981 |
| Investigational medicinal product code | |
| Other name | Subasumstat |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

| | |
|---|-----------------------|
| Dosage and administration details: | |
| TAK-981 120 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle. | |
| Investigational medicinal product name | Pembrolizumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:
Pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| Number of subjects in period 1^[1] | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab |
|---|--|--|--|
| Started | 3 | 6 | 33 |
| Completed | 2 | 2 | 9 |
| Not completed | 1 | 4 | 24 |
| Consent withdrawn by subject | - | - | 11 |
| Reason Not Specified | - | 1 | 1 |
| Progressive Disease | 1 | 3 | 12 |
| New anti-cancer therapy | - | - | - |
| Lost to follow-up | - | - | - |

| Number of subjects in period 1^[1] | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|---|---|
| Started | 19 |
| Completed | 4 |
| Not completed | 15 |
| Consent withdrawn by subject | 4 |
| Reason Not Specified | 1 |
| Progressive Disease | 8 |
| New anti-cancer therapy | 1 |
| Lost to follow-up | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial because this is a two-phase study wherein participants were newly recruited in each phase.

Period 2

| | |
|------------------------------|--------------------------|
| Period 2 title | Phase 2 (Dose Expansion) |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

The arms in Period 2: Dose Expansion are mutually exclusive. However, due to database limitation which does not allow a greater number of participants to be present in the subsequent period [as compared to the preceding period], an alternative selection has been made.

Arms

| | |
|------------------------------|----|
| Are arms mutually exclusive? | No |
|------------------------------|----|

| | |
|------------------|--|
| Arm title | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg |
|------------------|--|

Arm description:

Participants with non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

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

Dosage and administration details:

Pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|--|-----------------------|
| Investigational medicinal product name | TAK-981 |
| Investigational medicinal product code | |
| Other name | Subasumstat |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

TAK-981 40 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle.

| | |
|------------------|---|
| Arm title | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg |
|------------------|---|

Arm description:

Participants with non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | TAK-981 |
| Investigational medicinal product code | |
| Other name | Subasumstat |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

TAK-981 40 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle.

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

Dosage and administration details:

Pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|------------------|---|
| Arm title | Dose Expansion: Cohort B: Cervical Cancer |
|------------------|---|

Arm description:

Participants with cervical cancer received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

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

| | |
|--|-----------------------|
| Investigational medicinal product name | TAK-981 |
| Investigational medicinal product code | |
| Other name | Subasumstat |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

TAK-981 40 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle.

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

Dosage and administration details:

Pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|------------------|-----------------------------------|
| Arm title | Dose Expansion: Cohort C: MSS-CRC |
|------------------|-----------------------------------|

Arm description:

Participants with MSS-CRC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | TAK-981 |
| Investigational medicinal product code | |
| Other name | Subasumstat |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

TAK-981 40 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle.

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

Dosage and administration details:

Pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|------------------|--|
| Arm title | Dose Expansion: Cohort D: Cutaneous Melanoma |
|------------------|--|

Arm description:

Participants with cutaneous melanoma received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | TAK-981 |
| Investigational medicinal product code | |
| Other name | Subasumstat |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

TAK-981 40 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle.

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

Dosage and administration details:

Pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|------------------|--|
| Arm title | Dose Expansion: Cohort E: Squamous NSCLC |
|------------------|--|

Arm description:

Participants with squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | TAK-981 |
| Investigational medicinal product code | |
| Other name | Subasumstat |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

TAK-981 40 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle.

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

Dosage and administration details:

Pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|------------------|--|
| Arm title | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC |
|------------------|--|

Arm description:

Participants with CPI refractory squamous or non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | TAK-981 |
| Investigational medicinal product code | |
| Other name | Subasumstat |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

TAK-981 40 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle.

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

Dosage and administration details:

Pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| Number of subjects in period 2 | Dose Expansion: Cohort A: Non- squamous NSCLC TAK-981 90 mg | Dose Expansion: Cohort A: Non- squamous NSCLC TAK-981 120 mg | Dose Expansion: Cohort B: Cervical Cancer |
|--------------------------------|--|---|---|
| | | | |
| Started | 14 | 9 | 21 |
| Completed | 8 | 5 | 17 |
| Not completed | 6 | 4 | 4 |
| Consent withdrawn by subject | 1 | 2 | 4 |
| Reason Not Specified | - | - | - |
| Progressive Disease | 2 | 1 | - |
| New anti-cancer therapy | 3 | 1 | - |
| Lost to follow-up | - | - | - |

| Number of subjects in period 2 | Dose Expansion: Cohort C: MSS-CRC | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort E: Squamous NSCLC |
|--------------------------------|--------------------------------------|--|--|
| | | | |
| Started | 9 | 28 | 15 |
| Completed | 2 | 23 | 4 |
| Not completed | 7 | 5 | 11 |
| Consent withdrawn by subject | 2 | 1 | 4 |
| Reason Not Specified | 1 | - | - |
| Progressive Disease | 3 | 3 | 4 |
| New anti-cancer therapy | - | - | 2 |
| Lost to follow-up | 1 | 1 | 1 |

| Number of subjects in period 2 | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC |
|--------------------------------|---|
| Started | 4 |
| Completed | 1 |
| Not completed | 3 |
| Consent withdrawn by subject | 1 |
| Reason Not Specified | - |
| Progressive Disease | 2 |
| New anti-cancer therapy | - |
| Lost to follow-up | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Dose Escalation: TAK-981 40 mg + Pembrolizumab |
|-----------------------|--|

Reporting group description:

Participants received TAK-981 40 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months).

| | |
|-----------------------|--|
| Reporting group title | Dose Escalation: TAK-981 60 mg + Pembrolizumab |
|-----------------------|--|

Reporting group description:

Participants received TAK-981 60 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months).

| | |
|-----------------------|--|
| Reporting group title | Dose Escalation: TAK-981 90 mg + Pembrolizumab |
|-----------------------|--|

Reporting group description:

Participants received TAK-981 90 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months).

| | |
|-----------------------|---|
| Reporting group title | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|-----------------------|---|

Reporting group description:

Participants received TAK-981, 120 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months).

| Reporting group values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab |
|------------------------------------|--|--|--|
| Number of subjects | 3 | 6 | 33 |
| Age Categorical Units: Subjects | | | |

| | | | |
|---|--------|--------|---------|
| Age continuous Units: years | | | |
| arithmetic mean | 66.0 | 53.5 | 56.2 |
| standard deviation | ± 5.57 | ± 7.23 | ± 11.91 |
| Gender categorical Units: Subjects | | | |
| Female | 1 | 5 | 16 |
| Male | 2 | 1 | 17 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 4 | 8 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 3 |
| White | 3 | 2 | 17 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 5 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 2 | 1 | 6 |

| | | | |
|-------------------------|---|---|----|
| Not Hispanic or Latino | 1 | 5 | 25 |
| Unknown or Not Reported | 0 | 0 | 2 |

| Reporting group values | Dose Escalation: TAK-981 120 mg + Pembrolizumab | Total | |
|------------------------------------|---|-------|--|
| Number of subjects | 19 | 61 | |
| Age Categorical Units: Subjects | | | |

| | | | |
|---|-----------------|----|--|
| Age continuous Units: years arithmetic mean standard deviation | 59.8 ± 13.32 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 8 | 30 | |
| Male | 11 | 31 | |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 7 | 19 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 1 | 4 | |
| White | 9 | 31 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 2 | 7 | |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 1 | 10 | |
| Not Hispanic or Latino | 18 | 49 | |
| Unknown or Not Reported | 0 | 2 | |

Subject analysis sets

| | |
|----------------------------|--|
| Subject analysis set title | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants with non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|---|
| Subject analysis set title | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants with non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|---|
| Subject analysis set title | Dose Expansion: Cohort B: Cervical Cancer |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants with cervical cancer received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|-----------------------------------|
| Subject analysis set title | Dose Expansion: Cohort C: MSS-CRC |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants with MSS-CRC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|--|
| Subject analysis set title | Dose Expansion: Cohort D: Cutaneous Melanoma |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants with cutaneous melanoma received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|--|
| Subject analysis set title | Dose Expansion: Cohort E: Squamous NSCLC |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants with squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|--|
| Subject analysis set title | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC |
| Subject analysis set type | Full analysis |

Subject analysis set description:

Participants with CPI refractory squamous or non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| Reporting group values | Dose Expansion: Cohort A: Non- squamous NSCLC TAK-981 90 mg | Dose Expansion: Cohort A: Non- squamous NSCLC TAK-981 120 mg | Dose Expansion: Cohort B: Cervical Cancer |
|------------------------------------|--|---|---|
| Number of subjects | 14 | 9 | 21 |
| Age Categorical Units: Subjects | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| Age continuous Units: years arithmetic mean standard deviation | 63.3 ± 10.83 | 68.7 ± 9.12 | 51.8 ± 13.24 |
| Gender categorical Units: Subjects | | | |
| Female | 6 | 5 | 21 |
| Male | 8 | 4 | 0 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 3 | 1 | 2 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 1 | 0 | 0 |

| | | | |
|-------------------------|----|---|----|
| White | 10 | 8 | 17 |
| More than one race | 0 | 0 | 2 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 5 | 0 | 12 |
| Not Hispanic or Latino | 8 | 9 | 9 |
| Unknown or Not Reported | 1 | 0 | 0 |

| Reporting group values | Dose Expansion: Cohort C: MSS-CRC | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort E: Squamous NSCLC |
|------------------------|--------------------------------------|--|--|
| Number of subjects | 9 | 28 | 15 |
| Age Categorical | | | |
| Units: Subjects | | | |

| | | | |
|--|--------|---------|--------|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 49.6 | 55.9 | 67.5 |
| standard deviation | ± 9.22 | ± 13.95 | ± 7.66 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 5 | 12 | 1 |
| Male | 4 | 16 | 14 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 1 | 4 | 5 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 1 | 0 | 0 |
| White | 7 | 23 | 10 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 1 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 14 | 0 |
| Not Hispanic or Latino | 9 | 14 | 14 |
| Unknown or Not Reported | 0 | 0 | 1 |

| Reporting group values | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC | | |
|------------------------|---|--|--|
| Number of subjects | 4 | | |
| Age Categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------|--------|--|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 73.5 | | |
| standard deviation | ± 3.70 | | |

| | | | |
|---|---|--|--|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 1 | | |
| Male | 3 | | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | | |
| Asian | 0 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 0 | | |
| White | 4 | | |
| More than one race | 0 | | |
| Unknown or Not Reported | 0 | | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | | |
| Not Hispanic or Latino | 4 | | |
| Unknown or Not Reported | 0 | | |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Dose Escalation: TAK-981 40 mg + Pembrolizumab |
| Reporting group description: Participants received TAK-981 40 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months). | |
| Reporting group title | Dose Escalation: TAK-981 60 mg + Pembrolizumab |
| Reporting group description: Participants received TAK-981 60 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months). | |
| Reporting group title | Dose Escalation: TAK-981 90 mg + Pembrolizumab |
| Reporting group description: Participants received TAK-981 90 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months). | |
| Reporting group title | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
| Reporting group description: Participants received TAK-981, 120 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months). | |
| Reporting group title | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg |
| Reporting group description: Participants with non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months. | |
| Reporting group title | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg |
| Reporting group description: Participants with non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months. | |
| Reporting group title | Dose Expansion: Cohort B: Cervical Cancer |
| Reporting group description: Participants with cervical cancer received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months. | |
| Reporting group title | Dose Expansion: Cohort C: MSS-CRC |
| Reporting group description: Participants with MSS-CRC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months. | |
| Reporting group title | Dose Expansion: Cohort D: Cutaneous Melanoma |
| Reporting group description: Participants with cutaneous melanoma received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months. | |
| Reporting group title | Dose Expansion: Cohort E: Squamous NSCLC |
| Reporting group description: Participants with squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 | |

and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|-----------------------|--|
| Reporting group title | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC |
|-----------------------|--|

Reporting group description:

Participants with CPI refractory squamous or non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|--|
| Subject analysis set title | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg |
|----------------------------|--|

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

Subject analysis set description:

Participants with non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|---|
| Subject analysis set title | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg |
|----------------------------|---|

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

Subject analysis set description:

Participants with non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|---|
| Subject analysis set title | Dose Expansion: Cohort B: Cervical Cancer |
|----------------------------|---|

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

Subject analysis set description:

Participants with cervical cancer received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|-----------------------------------|
| Subject analysis set title | Dose Expansion: Cohort C: MSS-CRC |
|----------------------------|-----------------------------------|

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

Subject analysis set description:

Participants with MSS-CRC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|--|
| Subject analysis set title | Dose Expansion: Cohort D: Cutaneous Melanoma |
|----------------------------|--|

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

Subject analysis set description:

Participants with cutaneous melanoma received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|--|
| Subject analysis set title | Dose Expansion: Cohort E: Squamous NSCLC |
|----------------------------|--|

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

Subject analysis set description:

Participants with squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|----------------------------|--|
| Subject analysis set title | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC |
|----------------------------|--|

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

Subject analysis set description:

Participants with CPI refractory squamous or non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

Primary: Phase 1: Number of Participants With One or More Treatment Emergent Adverse Events (TEAEs)

| | |
|-----------------|---|
| End point title | Phase 1: Number of Participants With One or More Treatment Emergent Adverse Events (TEAEs) ^[1] |
|-----------------|---|

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant administered a medicinal investigational drug. The untoward medical occurrence does not necessarily have to have a causal relationship with treatment. A TEAE is defined as an AE that occurs after administration of first dose of study drug and through 30 days after last dose of study drug or until start of subsequent antineoplastic therapy. AEs were evaluated according to National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), Version 5.0 except cytokine release syndrome (CRS), which was graded according to American Society for Transplantation and Cellular Therapy (ASTCT) Consensus Grading for CRS. Safety Analysis Set included participants who received at least 1 dose, even if incomplete, of study drug.

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

End point timeframe:

Up to approximately 24 months

Notes:

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

Justification: Only descriptive analysis were planned for this endpoint.

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|-----------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 33 | 19 |
| Units: participants | 3 | 6 | 33 | 19 |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants With One or More Serious Adverse Events (SAEs)

| | |
|-----------------|---|
| End point title | Phase 1: Number of Participants With One or More Serious Adverse Events (SAEs) ^[2] |
|-----------------|---|

End point description:

An SAE is any untoward medical occurrence that results in death; is life-threatening; requires inpatient hospitalization or prolongation of present hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect or is a medically important event that may not be immediately life-threatening or result in death or hospitalization, but may jeopardize the participant or may require intervention to prevent one of other outcomes listed in definition above, or involves suspected transmission via a medicinal product of an infectious agent. Safety Analysis Set included participants who received at least 1 dose, even if incomplete, of study drug.

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

End point timeframe:

Up to approximately 24 months

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: Only descriptive analysis were planned for this endpoint.

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|-----------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 33 | 19 |
| Units: participants | 0 | 3 | 17 | 10 |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants With Dose Limiting Toxicities (DLTs)

| | |
|-----------------|---|
| End point title | Phase 1: Number of Participants With Dose Limiting Toxicities (DLTs) ^[3] |
|-----------------|---|

End point description:

DLTs were evaluated according to NCI CTCAE Version 5.0 except CRS, which was graded according to ASTCT Consensus Grading for CRS. The DLT-evaluable Analysis Set included participants enrolled in Phase 1b of the study and who experienced a DLT at any time after receiving the first dose of TAK-981 during the DLT assessment period (Cycle 1) or who received all planned TAK-981 doses and 1 administration of pembrolizumab in Cycle 1.

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

End point timeframe:

Up to Cycle 1 (each cycle was of 21 days)

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: Only descriptive analysis were planned for this endpoint.

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|-----------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 30 | 19 |
| Units: participants | 0 | 0 | 2 | 1 |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants With Grade 3 or Higher Treatment Emergent Adverse Events (TEAEs)

| | |
|-----------------|---|
| End point title | Phase 1: Number of Participants With Grade 3 or Higher Treatment Emergent Adverse Events (TEAEs) ^[4] |
|-----------------|---|

End point description:

AE means any untoward medical occurrence in a participant administered a pharmaceutical product. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product whether or not it is related to the medicinal product. A TEAE was defined as an adverse event which occurred on or after the first dose of study drug and no more than 30

days after the last dose of study drug. A severity grade was evaluated as per the NCI CTCAE Version 5.0, except for CRS, which was assessed by ASTCT Consensus Grading for CRS. DLTs were evaluated according to NCI CTCAE Version 5.0 except CRS, which was graded according to ASTCT Consensus Grading for CRS. Safety Analysis Set included participants who received at least 1 dose, even if incomplete, of study drug.

Reporting Groups

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

End point timeframe:

Up to approximately 24 months

Notes:

[4] - 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: Only descriptive analysis were planned for this endpoint.

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|-----------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 33 | 19 |
| Units: participants | 0 | 2 | 20 | 15 |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Overall Response Rate (ORR) as Assessed by the Investigator According to RECIST, Version 1.1

| | |
|-----------------|--|
| End point title | Phase 2: Overall Response Rate (ORR) as Assessed by the Investigator According to RECIST, Version 1.1 ^[5] |
|-----------------|--|

End point description:

ORR is defined as the percentage of participants who achieve Complete Response (CR) and Partial Response (PR) (determined by the investigator) during the study according to Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1. Response-Evaluable Analysis Set included participants who had received at least 1 dose of study drug, had sites of measurable disease at baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happened.

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

End point timeframe:

Up to approximately 25 months

Notes:

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

Justification: Only descriptive analysis were planned for this endpoint.

| End point values | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg | Dose Expansion: Cohort B: Cervical Cancer | Dose Expansion: Cohort C: MSS-CRC |
|-----------------------------------|--|---|---|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 10 | 8 | 20 | 9 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 20 (2.52 to | 0 (0.00 to | 30 (11.89 to | 0 (0.00 to |

| | | | |
|--------|--------|--------|--------|
| 55.61) | 36.94) | 54.28) | 33.63) |
|--------|--------|--------|--------|

| End point values | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort E: Squamous NSCLC | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC | |
|-----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 13 | 4 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 25 (10.69 to 44.87) | 7.7 (0.19 to 36.03) | 0 (0.00 to 60.24) | |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants with One or More TEAEs Leading to Dose Modifications and Treatment Discontinuation

| | |
|-----------------|---|
| End point title | Phase 1: Number of Participants with One or More TEAEs Leading to Dose Modifications and Treatment Discontinuation ^[6] |
|-----------------|---|

End point description:

An AE is any untoward medical occurrence in a participant administered a medicinal investigational drug. The untoward medical occurrence does not necessarily have to have a causal relationship with treatment. A TEAE is defined as an AE that occurs after administration of first dose of study drug and through 30 days after last dose of study drug or until start of subsequent antineoplastic therapy. Pembrolizumab is denoted as Pem. Safety Analysis Set included participants who received at least 1 dose, even if incomplete, of study drug.

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

End point timeframe:

Up to approximately 24 months

Notes:

[6] - 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: Only descriptive analysis were planned for this endpoint.

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|---|---|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 33 | 19 |
| Units: participants | | | | |
| TEAE Resulting in Dose Modifications of TAK-981 | 0 | 3 | 22 | 11 |
| TEAE Resulting in Dose Modifications of Pem | 0 | 3 | 15 | 4 |
| TEAE Resulting in Drug Discontinuation of TAK-981 | 0 | 1 | 3 | 2 |
| TEAE Resulting in Drug Discontinuation of Pem | 0 | 1 | 4 | 1 |

Statistical analyses

No statistical analyses for this end point

Primary: Phase 1: Number of Participants With Clinically Significant Laboratory Values

| | |
|-----------------|--|
| End point title | Phase 1: Number of Participants With Clinically Significant Laboratory Values ^[7] |
|-----------------|--|

End point description:

Laboratory parameters included clinical chemistry, hematology, and urinalysis. Participants with at least 1 Grade 3 or 4 Lab Abnormalities were reported. Safety Analysis Set included participants who received at least 1 dose, even if incomplete, of study drug.

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

End point timeframe:

Up to approximately 24 months

Notes:

[7] - 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: Only descriptive analysis were planned for this endpoint.

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|-----------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 33 | 19 |
| Units: participants | | | | |
| Hematology | 1 | 3 | 7 | 6 |
| Serum Chemistry | 1 | 1 | 7 | 5 |
| Coagulation | 0 | 0 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Tmax: Time to Reach the Maximum Plasma Concentration (Cmax) for TAK-981

| | |
|-----------------|--|
| End point title | Phase 1: Tmax: Time to Reach the Maximum Plasma Concentration (Cmax) for TAK-981 |
|-----------------|--|

End point description:

PK Analysis Set included participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. 'n' denotes number of participants available for analysis during the specified time-point.

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

End point timeframe:

Cycle 1 (each cycle is 21 days) Days 1 and 8 pre-dose and at multiple timepoints (up to 24 hours)

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|-------------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 33 | 19 |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 1(n=3,6,33,19) | 1.22 (1.20 to 1.23) | 1.27 (1.00 to 1.47) | 1.17 (1.00 to 1.88) | 1.20 (1.00 to 1.72) |
| Cycle 1 Day 8(n=3,6,30,17) | 1.18 (1.17 to 1.25) | 1.41 (1.00 to 1.70) | 1.22 (1.00 to 3.10) | 1.28 (0.98 to 1.50) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Cmax: Maximum Observed Plasma Concentration for TAK-981

| | |
|-----------------|--|
| End point title | Phase 1: Cmax: Maximum Observed Plasma Concentration for TAK-981 |
|-----------------|--|

End point description:

Pharmacokinetic (PK) Analysis Set included participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. 'n' denotes number of participants available for analysis during the specified time-point.

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

End point timeframe:

Cycle 1 (each cycle is 21 days) Days 1 and 8 pre-dose and at multiple timepoints (up to 24 hours)

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|---|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 33 | 19 |
| Units: nanograms per milliliter (ng/ml) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1(n=3,6,33,19) | 335 (± 282) | 728 (± 396) | 888 (± 423) | 1290 (± 571) |
| Cycle 1 Day 8(n=3,6,30,17) | 280 (± 167) | 448 (± 206) | 780 (± 524) | 1270 (± 770) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: AUC_{0-t}: Area Under the Plasma Concentration-time Curve from Time 0 to Time t Over the Dosing Interval for TAK-981

| | |
|-----------------|---|
| End point title | Phase 1: AUC _{0-t} : Area Under the Plasma Concentration-time Curve from Time 0 to Time t Over the Dosing Interval for TAK-981 |
|-----------------|---|

End point description:

PK Analysis Set included participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Subjects analyzed is the number of participants with data available for analysis. 'n' denotes number of participants available for analysis during the specified time-point.

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

End point timeframe:

Cycle 1 (each cycle is 21 days) Days 1 and 8 pre-dose and at multiple timepoints (up to 24 hours)

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|--------------------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 32 | 18 |
| Units: hours*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1(n=3,6,32,18) | 880 (± 427) | 1370 (± 517) | 1950 (± 735) | 2580 (± 949) |
| Cycle 1 Day 8(n=3,5,28,16) | 814 (± 290) | 976 (± 232) | 1780 (± 908) | 2640 (± 1260) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: AUC_∞: Area Under the Plasma Concentration-time Curve from Time 0 to Infinity for TAK-981

| | |
|-----------------|--|
| End point title | Phase 1: AUC _∞ : Area Under the Plasma Concentration-time Curve from Time 0 to Infinity for TAK-981 |
|-----------------|--|

End point description:

PK Analysis Set included participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Subjects analyzed is the number of participants with data available for analysis. 'n' denotes number of participants available for analysis during the specified time-point.

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

End point timeframe:

Cycle 1 (each cycle is 21 days) Days 1 and 8 pre-dose and at multiple timepoints (up to 24 hours)

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|--------------------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 32 | 17 |
| Units: hours*ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1(n=3,6,32,17) | 909 (± 432) | 1400 (± 530) | 2020 (± 760) | 2660 (± 1020) |
| Cycle 1 Day 8(n=3,5,27,16) | 845 (± 292) | 1010 (± 233) | 1830 (± 942) | 2750 (± 1320) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: CL: Total Clearance After Intravenous Administration for TAK-981

| | |
|---|---|
| End point title | Phase 1: CL: Total Clearance After Intravenous Administration for TAK-981 |
| End point description: PK Analysis Set included participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Subjects analyzed is the number of participants with data available for analysis. 'n' denotes number of participants available for analysis during the specified time-point. | |
| End point type | Secondary |
| End point timeframe: Cycle 1 (each cycle is 21 days) Days 1 and 8 pre-dose and at multiple timepoints (up to 24 hours) | |

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|--------------------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 32 | 17 |
| Units: liters per hour (L/h) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1(n=3,6,32,17) | 51.1 (± 23.2) | 47.2 (± 14.8) | 51.3 (± 19.6) | 51.0 (± 18.4) |
| Cycle 1 Day 8(n=3,5,27,16) | 51.7 (± 19.3) | 62.5 (± 15.5) | 57.0 (± 21.8) | 53.8 (± 26.8) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: t1/2z: Terminal Disposition Phase Half-life for TAK-981

| | |
|-----------------|--|
| End point title | Phase 1: t1/2z: Terminal Disposition Phase Half-life for TAK-981 |
|-----------------|--|

End point description:

PK Analysis Set included participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Subjects analyzed is the number of participants with data available for analysis. 'n' denotes number of participants available for analysis during the specified time-point.

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

End point timeframe:

Cycle 1 (each cycle is 21 days) Days 1 and 8 pre-dose and at multiple timepoints (up to 24 hours)

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|-------------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 32 | 17 |
| Units: hours | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 Day 1(n=3,6,32,17) | 5.88 (5.82 to 6.16) | 5.58 (5.04 to 6.03) | 5.72 (3.31 to 10.43) | 6.79 (5.93 to 8.14) |
| Cycle 1 Day 8(n=3,5,27,16) | 5.83 (5.69 to 6.33) | 5.68 (5.22 to 6.44) | 6.06 (4.18 to 9.13) | 6.67 (5.26 to 8.08) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Vss: Volume of Distribution at Steady State After Intravenous Administration for TAK-981

| | |
|-----------------|---|
| End point title | Phase 1: Vss: Volume of Distribution at Steady State After Intravenous Administration for TAK-981 |
|-----------------|---|

End point description:

PK Analysis Set included participants with sufficient dosing and PK data to reliably estimate 1 or more PK parameters. Subjects analyzed is the number of participants with data available for analysis. 'n' denotes number of participants available for analysis during the specified time-point.

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

End point timeframe:

Cycle 1 (each cycle is 21 days) Days 1 and 8 pre-dose and at multiple timepoints (up to 24 hours)

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|--------------------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 32 | 17 |
| Units: liters (L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1(n=3,6,32,17) | 312 (± 203) | 181 (± 56.9) | 240 (± 115) | 240 (± 98.5) |

| | | | | |
|----------------------------|-------------|-------------|-------------|-------------|
| Cycle 1 Day 8(n=3,5,27,16) | 323 (± 178) | 314 (± 109) | 300 (± 129) | 271 (± 150) |
|----------------------------|-------------|-------------|-------------|-------------|

Statistical analyses

No statistical analyses for this end point

Secondary: Phases 1 and 2: Disease Control Rate (DCR)

| | |
|---|--|
| End point title | Phases 1 and 2: Disease Control Rate (DCR) |
| End point description: | |
| DCR is defined as the percentage of participants who achieved stable disease (SD) or better (CR + PR + SD determined by the investigator) >6 weeks during the trial in the response-evaluable population. Response-Evaluable Analysis Set included participants who had received at least 1 dose of study drug, had sites of measurable disease at baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happened. | |
| End point type | Secondary |
| End point timeframe: | |
| Phase 1: Up to approximately 24 months, Phase 2: Up to approximately 25 months | |

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg |
|-----------------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 10 | 6 | 8 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 33.3 (0.84 to 90.57) | 80.0 (44.39 to 97.48) | 50.0 (11.81 to 88.19) | 62.5 (24.49 to 91.48) |

| End point values | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Expansion: Cohort B: Cervical Cancer | Dose Escalation: TAK-981 120 mg + Pembrolizumab | Dose Expansion: Cohort C: MSS-CRC |
|-----------------------------------|--|---|---|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 33 | 20 | 18 | 9 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 30.3 (15.59 to 48.71) | 55.0 (31.53 to 76.94) | 44.4 (21.53 to 69.24) | 22.2 (2.81 to 60.01) |

| End point values | Dose Expansion: Cohort D: | Dose Expansion: Cohort E: | Dose Expansion: Cohort F: CPI | |
|------------------|---------------------------|---------------------------|-------------------------------|--|
|------------------|---------------------------|---------------------------|-------------------------------|--|

| | Cutaneous Melanoma | Squamous NSCLC | Refractory Squamous or NSCLC | |
|-----------------------------------|-----------------------|----------------------|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 13 | 4 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 67.9 (47.65 to 84.12) | 30.8 (9.09 to 61.43) | 0 (0.00 to 60.24) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phases 1 and 2: Durable Response Rate (DRR)

| | |
|-----------------|---|
| End point title | Phases 1 and 2: Durable Response Rate (DRR) |
|-----------------|---|

End point description:

DRR is defined as the rate of objective responses (CR + PR) maintained for at least 6 months initiating at any time within 12 months of commencing therapy. Response-Evaluable Analysis Set included participants who had received at least 1 dose of study drug, had sites of measurable disease at baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happened.

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

End point timeframe:

Phase 1: Up to approximately 24 months, Phase 2: Up to approximately 25 months

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg |
|-----------------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 10 | 6 | 8 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 0 (0.00 to 70.76) | 10.0 (0.25 to 44.50) | 16.7 (0.42 to 64.12) | 0 (0.00 to 36.94) |

| End point values | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Expansion: Cohort B: Cervical Cancer | Dose Escalation: TAK-981 120 mg + Pembrolizumab | Dose Expansion: Cohort C: MSS-CRC |
|-----------------------------------|--|---|---|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 33 | 20 | 18 | 9 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 6.1 (0.74 to 20.23) | 0 (0.00 to 16.84) | 0 (0.00 to 18.53) | 0 (0.00 to 33.63) |

| End point values | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort E: Squamous NSCLC | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC | |
|-----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 13 | 4 | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 10.7 (2.27 to 28.23) | 0 (0.00 to 24.71) | 0 (0.00 to 60.24) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phases 1 and 2: Duration of Response (DOR)

| | |
|--|--|
| End point title | Phases 1 and 2: Duration of Response (DOR) |
| End point description: | |
| DOR is defined as a time from the time of first documentation of tumor response to the first recorded occurrence of disease progression (PD) or death from any cause (whichever occurs first), through end of study. Response-Evaluable Analysis Set included participants who had received at least 1 dose of study drug, had sites of measurable disease at baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happened. Subjects analysed is the number of participants with events. '-999' and '999' denotes lower and upper limit of 95% Confidence Interval (CI) was not estimable for a single participant. '99999' denotes upper limit of 95% CI was not estimable due to censoring. '9999' denotes median and upper limit of 95% CI was not estimable due to censoring. | |
| End point type | Secondary |
| End point timeframe: | |
| Phase 1: Up to approximately 24 months, Phase 2: Up to approximately 25 months | |

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Expansion: Cohort A: Non- squamous NSCLC TAK- 981 90 mg | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Expansion: Cohort A: Non- squamous NSCLC TAK- 981 120 mg |
|----------------------------------|---|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[8] | 1 | 1 | 0 ^[9] |
| Units: hours | | | | |
| median (confidence interval 95%) | (to) | 7.62 (-999 to 999) | 17.12 (-999 to 999) | (to) |

Notes:

[8] - No participants with the event were available for analysis.

[9] - No participants with events were available for analysis.

| End point values | Dose Escalation: | Dose Expansion: | Dose Escalation: | Dose Expansion: |
|------------------|------------------|-----------------|------------------|-----------------|
|------------------|------------------|-----------------|------------------|-----------------|

| | TAK-981 90 mg + Pembrolizumab | Cohort B: Cervical Cancer | TAK-981 120 mg + Pembrolizumab | Cohort C: MSS-CRC |
|----------------------------------|-------------------------------|---------------------------|--------------------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 2 | 1 | 0 ^[10] |
| Units: hours | | | | |
| median (confidence interval 95%) | 7.39 (4.17 to 99999) | 9999 (4.67 to 9999) | 3.71 (-999 to 999) | (to) |

Notes:

[10] - No participants with events were available for analysis.

| End point values | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort E: Squamous NSCLC | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 3 | 1 | 0 ^[11] | |
| Units: hours | | | | |
| median (confidence interval 95%) | 9999 (7.26 to 9999) | 4.34 (-999 to 999) | (to) | |

Notes:

[11] - No participants with events were available for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Phases 1 and 2: Progression-free Survival (PFS)

| | |
|-----------------|---|
| End point title | Phases 1 and 2: Progression-free Survival (PFS) |
|-----------------|---|

End point description:

PFS is defined as time from the date of the first dose administration to the date of first documentation of PD or death due to any cause whichever occurs first, through the end of the study. Response-Evaluable Analysis Set included participants who had received at least 1 dose of study drug, had sites of measurable disease at baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happened. Subjects analysed is the number of participants with events. '-999' and '999' denotes lower and upper limit of 95% CI was not estimable for a single participant. '99999' denotes upper limit of 95% CI was not estimable due to censoring.

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

End point timeframe:

Phase 1: Up to approximately 24 months, Phase 2: Up to approximately 25 months

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg |
|----------------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 8 | 5 | 7 |
| Units: months | | | | |
| median (confidence interval 95%) | 2.00 (2.00 to) | 3.71 (3.29 to) | 4.21 (2.00 to) | 4.59 (1.97 to) |

| | | | |
|--------|-------|--------|--------|
| 99999) | 9.20) | 99999) | 99999) |
|--------|-------|--------|--------|

| End point values | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Expansion: Cohort B: Cervical Cancer | Dose Escalation: TAK-981 120 mg + Pembrolizumab | Dose Expansion: Cohort C: MSS-CRC |
|----------------------------------|--|---|---|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 28 | 15 | 16 | 8 |
| Units: months | | | | |
| median (confidence interval 95%) | 1.99 (1.77 to 3.91) | 4.14 (2.14 to 8.87) | 2.11 (1.41 to 6.57) | 1.64 (1.28 to 2.00) |

| End point values | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort E: Squamous NSCLC | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 17 | 11 | 4 | |
| Units: months | | | | |
| median (confidence interval 95%) | 8.97 (2.37 to 12.42) | 2.07 (1.87 to 2.30) | 1.28 (0.99 to 999) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phases 1 and 2: Time to Response (TTR)

| | |
|-----------------|--|
| End point title | Phases 1 and 2: Time to Response (TTR) |
|-----------------|--|

End point description:

TTR is defined as time from the date of the first dose administration to the date of first documented PR or better. Response-Evaluable Analysis Set included participants who had received at least 1 dose of study drug, had sites of measurable disease at baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happened. Subjects analysed is the number of participants with events. '99999' denotes upper limit of 95% CI was not estimable due to censoring. '9999' denotes median and upper limit of 95% CI was not estimable due to censoring. '9999', '-9999' and '9999' denotes median, lower limit and upper limit of 95% CI was not estimable due to censoring.

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

End point timeframe:

Phase 1: Up to approximately 24 months, Phase 2: Up to approximately 25 months

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg |
|----------------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 0 ^[12] | 2 | 2 | 0 ^[13] |
| Units: months | | | | |
| median (confidence interval 95%) | (to) | 4.01 (3.98 to 99999) | 4.17 (1.91 to 99999) | (to) |

Notes:

[12] - No participants with the event were available for analysis.

[13] - No participants with events were available for analysis.

| End point values | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Expansion: Cohort B: Cervical Cancer | Dose Escalation: TAK-981 120 mg + Pembrolizumab | Dose Expansion: Cohort C: MSS-CRC |
|----------------------------------|--|---|---|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 1 | 0 ^[14] |
| Units: months | | | | |
| median (confidence interval 95%) | 99999 (3.94 to 99999) | 6.01 (4.04 to 99999) | 9999 (-9999 to 9999) | (to) |

Notes:

[14] - No participants with events were available for analysis.

| End point values | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort E: Squamous NSCLC | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 7 | 1 | 0 ^[15] | |
| Units: months | | | | |
| median (confidence interval 95%) | 99999 (-99999 to 99999) | 99999 (-99999 to 99999) | (to) | |

Notes:

[15] - No participants with events were available for analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Overall Survival (OS)

| | |
|-----------------|--------------------------------|
| End point title | Phase 2: Overall Survival (OS) |
|-----------------|--------------------------------|

End point description:

OS is defined as the time from the date of the first dose administration to the date of death. Participants without documentation of death at the time of analysis were censored at the date last known to be alive. Response-Evaluable Analysis Set included participants who had received at least 1 dose of study drug, had sites of measurable disease at baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happened. Subjects analysed is the number of participants with events. '99999' denotes upper limit of 95% CI was not estimable due to censoring. '9999' denotes median and upper limit of 95% CI was not estimable due to censoring. '9999', '-9999' and '9999' denotes median, lower limit and upper limit of 95% CI was not estimable due to censoring.

| | |
|-------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to approximately 25 months | |

| End point values | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg | Dose Expansion: Cohort B: Cervical Cancer | Dose Expansion: Cohort C: MSS-CRC |
|----------------------------------|---|--|--|--------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 1 | 4 | 9 | 2 |
| Units: months | | | | |
| median (confidence interval 95%) | 9999 (-9999 to 9999) | 10.12 (5.16 to 99999) | 14.55 (5.42 to 99999) | 9999 (4.21 to 9999) |

| End point values | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort E: Squamous NSCLC | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC | |
|----------------------------------|---|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 8 | 1 | 1 | |
| Units: months | | | | |
| median (confidence interval 95%) | 9999 (11.43 to 9999) | 9999 (-9999 to 9999) | 99999 (1.28 to 99999) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phases 1 and 2: Time to Progression (TTP)

| | |
|---|---|
| End point title | Phases 1 and 2: Time to Progression (TTP) |
| End point description: | |
| TTP is defined as the from the date of the first dose administration to the date of the first documentation of PD as defined by standard disease criteria. Response-Evaluable Analysis Set included participants who had received at least 1 dose of study drug, had sites of measurable disease at baseline, and 1 postbaseline disease assessment, or were discontinued due to symptomatic deterioration or death before a postbaseline evaluation happened. Subjects analysed is the number of participants with events. '99999' denotes upper limit of 95% CI was not estimable due to censoring. | |
| End point type | Secondary |
| End point timeframe: | |
| Phase 1: Up to approximately 24 months, Phase 2: Up to approximately 25 months | |

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg |
|----------------------------------|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 8 | 5 | 6 |
| Units: months | | | | |
| median (confidence interval 95%) | 2.00 (2.00 to 99999) | 3.71 (3.29 to 9.20) | 4.21 (2.00 to 99999) | 4.01 (1.97 to 99999) |

| End point values | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Expansion: Cohort B: Cervical Cancer | Dose Escalation: TAK-981 120 mg + Pembrolizumab | Dose Expansion: Cohort C: MSS-CRC |
|----------------------------------|--|---|---|-----------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 25 | 13 | 15 | 6 |
| Units: months | | | | |
| median (confidence interval 95%) | 2.07 (1.87 to 4.04) | 5.34 (2.20 to 8.87) | 2.07 (1.41 to 6.93) | 1.76 (1.28 to 99999) |

| End point values | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort E: Squamous NSCLC | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC | |
|----------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 14 | 11 | 4 | |
| Units: months | | | | |
| median (confidence interval 95%) | 9.17 (4.11 to 99999) | 2.07 (1.87 to 2.30) | 1.28 (0.99 to 99999) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Fold Change from Baseline in TAK-981-/Small Ubiquitin-like Modifier (SUMO) Adduct Formation in Peripheral Blood Lymphocytes

| | |
|-----------------|---|
| End point title | Fold Change from Baseline in TAK-981-/Small Ubiquitin-like Modifier (SUMO) Adduct Formation in Peripheral Blood Lymphocytes |
|-----------------|---|

End point description:

The level of TAK-981-SUMO adduct formation was evaluated by flow cytometry as the percentage of adduct formed in peripheral blood lymphocytes. Positive change denotes improvement. Pharmacodynamic Analysis Set included participants who provided evaluable blood samples (Cycle 1, Day 1 predose sample and at least 1 postdose sample). Subjects analysed is the number of participants with data available for analysis. 'n' denotes the number of participants available for analysis during the specified time-point.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Cycle 1 Day 1 (1 hour, 4 hours, 8 hours) and Day 8 (Pre-dose, 1 hour, 4 hours and 8 hours) (Cycle length = 21 days) | |

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|---|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 18 | 13 |
| Units: ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1: 1 Hour Post Dose(n=3,6,18,13) | 8.1 (± 1.06) | 7.0 (± 3.12) | 8.5 (± 3.38) | 8.4 (± 2.40) |
| Cycle 1 Day 1: 4 Hours Post Dose(n=3,6,18,13) | 5.1 (± 0.82) | 5.0 (± 1.90) | 6.0 (± 1.80) | 6.3 (± 1.70) |
| Cycle 1 Day 1: 6-8 Hours Post Dose(n=3,6,18,13) | 4.6 (± 0.61) | 4.5 (± 1.87) | 5.3 (± 1.58) | 5.5 (± 1.29) |
| Cycle 1 Day 8: Predose(n=3,6,16,12) | 3.5 (± 0.53) | 2.6 (± 0.96) | 2.7 (± 1.43) | 2.0 (± 0.68) |
| Cycle 1 Day 8: 1 Hour Post Dose(n=3,6,16,10) | 11.9 (± 3.52) | 7.7 (± 2.88) | 9.2 (± 4.68) | 8.7 (± 2.01) |
| Cycle 1 Day 8: 4 Hours Post Dose(n=3,6,14,11) | 7.5 (± 1.52) | 6.0 (± 2.66) | 6.4 (± 2.90) | 6.1 (± 2.12) |
| Cycle 1 Day 8: 6-8 Hours Post Dose(n=3,6,14,11) | 6.5 (± 1.08) | 5.1 (± 2.30) | 5.7 (± 2.64) | 5.6 (± 1.96) |

Statistical analyses

No statistical analyses for this end point

Secondary: Fold Change from Baseline in SUMO 2/3 Inhibition in Peripheral Blood Lymphocytes

| | |
|---|--|
| End point title | Fold Change from Baseline in SUMO 2/3 Inhibition in Peripheral Blood Lymphocytes |
| End point description: | |
| SUMO pathway inhibition in blood was evaluated by flow cytometry in peripheral blood lymphocytes with an antibody recognizing SUMO 2/3 chains. Pharmacodynamic Analysis Set included participants who provided evaluable blood samples (Cycle 1, Day 1 predose sample and at least 1 postdose sample). Subjects analysed is the number of participants with data available for analysis. 'n' denotes the number of participants available for analysis during the specified time-point. | |
| End point type | Secondary |
| End point timeframe: | |
| Cycle 1 Day 1 (1 hour, 4 hours, 8 hours) and Day 8 (Pre-dose, 1 hour, 4 hours and 8 hours) (Cycle length = 21 days) | |

| End point values | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|---|--|--|--|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 6 | 18 | 13 |
| Units: ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1: 1 Hour Post Dose(n=3,6,18,13) | 0.7 (± 0.14) | 0.6 (± 0.21) | 0.6 (± 0.18) | 0.5 (± 0.08) |
| Cycle 1 Day 1: 4 Hours Post Dose(n=3,6,18,13) | 0.8 (± 0.07) | 0.6 (± 0.12) | 0.9 (± 0.54) | 0.6 (± 0.11) |
| Cycle 1 Day 1: 6-8 Hours Post Dose(n=3,6,18,13) | 0.8 (± 0.08) | 0.7 (± 0.19) | 1.0 (± 0.68) | 0.7 (± 0.34) |
| Cycle 1 Day 8: Predose(n=3,6,16,12) | 0.9 (± 0.24) | 1.0 (± 0.35) | 0.9 (± 0.36) | 0.7 (± 0.39) |
| Cycle 1 Day 8: 1 Hour Post Dose(n=3,6,16,10) | 0.6 (± 0.14) | 0.6 (± 0.23) | 0.7 (± 0.34) | 0.4 (± 0.15) |
| Cycle 1 Day 8: 4 Hours Post Dose(n=3,6,14,11) | 0.7 (± 0.22) | 0.6 (± 0.15) | 0.8 (± 0.58) | 0.5 (± 0.17) |
| Cycle 1 Day 8: 6-8 Hours Post Dose(n=3,6,14,11) | 0.7 (± 0.29) | 0.6 (± 0.11) | 0.9 (± 0.53) | 0.6 (± 0.22) |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Percentage of Participants With One or More Treatment Emergent Adverse Events (TEAEs)

| | |
|--|--|
| End point title | Phase 2: Percentage of Participants With One or More Treatment Emergent Adverse Events (TEAEs) |
| End point description: | |
| An AE is any untoward medical occurrence in a participant administered a medicinal investigational drug. The untoward medical occurrence does not necessarily have to have a causal relationship with treatment. A TEAE is defined as an AE that occurs after administration of first dose of study drug and through 30 days after last dose of study drug or until start of subsequent antineoplastic therapy. AEs were evaluated according to NCI CTCAE, Version 5.0 except CRS, which was graded according to ASTCT Consensus Grading for CRS. Safety Analysis Set included participants who received at least 1 dose, even if incomplete, of study drug. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to approximately 25 months | |

| End point values | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg | Dose Expansion: Cohort B: Cervical Cancer | Dose Expansion: Cohort C: MSS-CRC |
|-----------------------------------|--|---|--|--------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 14 | 9 | 21 | 9 |
| Units: percentage of participants | | | | |
| number (not applicable) | 100 | 100 | 100 | 100 |

| End point values | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort E: Squamous NSCLC | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC | |
|-----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 15 | 4 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 100 | 93.3 | 100 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Participants with One or More TEAEs Leading to Dose Modifications and Treatment Discontinuation

| | |
|-----------------|--|
| End point title | Phase 2: Number of Participants with One or More TEAEs Leading to Dose Modifications and Treatment Discontinuation |
|-----------------|--|

End point description:

An AE is any untoward medical occurrence in a participant administered a medicinal investigational drug. The untoward medical occurrence does not necessarily have to have a causal relationship with treatment. A TEAE is defined as an AE that occurs after administration of first dose of study drug and through 30 days after last dose of study drug or until start of subsequent antineoplastic therapy. Pembrolizumab is denoted as Pem. Safety Analysis Set included participants who received at least 1 dose, even if incomplete, of study drug.

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

End point timeframe:

Up to approximately 25 months

| End point values | Dose Expansion: Cohort A: Non- squamous NSCLC TAK- 981 90 mg | Dose Expansion: Cohort A: Non- squamous NSCLC TAK- 981 120 mg | Dose Expansion: Cohort B: Cervical Cancer | Dose Expansion: Cohort C: MSS- CRC |
|---|--|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 14 | 9 | 21 | 9 |
| Units: participants | | | | |
| TEAE Resulting in Dose Modifications of TAK-981 | 11 | 6 | 15 | 5 |
| TEAE Resulting in Dose Modifications of Pem | 7 | 5 | 12 | 4 |
| TEAE Resulting in Drug Discontinuation of TAK-981 | 1 | 1 | 6 | 0 |
| TEAE Resulting in Drug Discontinuation of Pem | 1 | 3 | 4 | 0 |

| End point values | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort E: Squamous NSCLC | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC | |
|---|---|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 15 | 4 | |
| Units: participants | | | | |
| TEAE Resulting in Dose Modifications of TAK-981 | 15 | 6 | 4 | |
| TEAE Resulting in Dose Modifications of Pem | 13 | 2 | 4 | |
| TEAE Resulting in Drug Discontinuation of TAK-981 | 6 | 1 | 0 | |
| TEAE Resulting in Drug Discontinuation of Pem | 3 | 1 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Participants With Grade 3 or Higher Treatment Emergent Adverse Events (TEAEs)

| | |
|-----------------|--|
| End point title | Phase 2: Number of Participants With Grade 3 or Higher Treatment Emergent Adverse Events (TEAEs) |
|-----------------|--|

End point description:

An AE means any untoward medical occurrence in a participant administered a pharmaceutical product. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product whether or not it is related to the medicinal product. A TEAE was defined as an adverse event which occurred on or after the first dose of study drug and no more than 30 days after the last dose of study drug. A severity grade was evaluated as per the NCI CTCAE Version 5.0, except for CRS, which was assessed by ASTCT Consensus Grading for CRS. Safety Analysis Set included participants who received at least 1 dose, even if incomplete, of study drug.

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

End point timeframe:

Up to approximately 25 months

| End point values | Dose Expansion: Cohort A: Non- squamous NSCLC TAK- 981 90 mg | Dose Expansion: Cohort A: Non- squamous NSCLC TAK- 981 120 mg | Dose Expansion: Cohort B: Cervical Cancer | Dose Expansion: Cohort C: MSS- CRC |
|-----------------------------|--|---|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 14 | 9 | 21 | 9 |
| Units: participants | 7 | 5 | 18 | 8 |

| End point values | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort E: Squamous NSCLC | Dose Expansion: Cohort F: CPI Refractory Squamous or NSCLC | |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 15 | 4 | |
| Units: participants | 14 | 4 | 2 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Phase 1: Up to approximately 24 months, Phase 2: Up to approximately 25 months

Adverse event reporting additional description:

Safety Analysis Set included participants who received at least 1 dose, even if incomplete, of study drug.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 27.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Dose Escalation: TAK-981 40 mg + Pembrolizumab |
|-----------------------|--|

Reporting group description:

Participants received TAK-981 40 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months).

| | |
|-----------------------|---|
| Reporting group title | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 120 mg |
|-----------------------|---|

Reporting group description:

Participants with non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|-----------------------|---|
| Reporting group title | Dose Expansion: Cohort B: Cervical Cancer |
|-----------------------|---|

Reporting group description:

Participants with cervical cancer received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|-----------------------|--|
| Reporting group title | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg |
|-----------------------|--|

Reporting group description:

Participants with non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|-----------------------|--|
| Reporting group title | Dose Expansion: Cohort D: Cutaneous Melanoma |
|-----------------------|--|

Reporting group description:

Participants with cutaneous melanoma received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|-----------------------|---|
| Reporting group title | Dose Expansion: Cohort F: CPI Refractory Squamous/NSCLC |
|-----------------------|---|

Reporting group description:

Participants with CPI refractory squamous or non-squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|-----------------------|--|
| Reporting group title | Dose Expansion: Cohort E: Squamous NSCLC |
|-----------------------|--|

Reporting group description:

Participants with squamous NSCLC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Dose Expansion: Cohort C: MSS-CRC |
|-----------------------|-----------------------------------|

Reporting group description:

Participants with MSS-CRC received TAK-981 as IV infusion on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle up to disease progression or 24-months and pembrolizumab 200 mg IV infusion as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle for a maximum of 24 months.

| | |
|-----------------------|---|
| Reporting group title | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|-----------------------|---|

Reporting group description:

Participants received TAK-981, 120 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months).

| | |
|-----------------------|--|
| Reporting group title | Dose Escalation: TAK-981 90 mg + Pembrolizumab |
|-----------------------|--|

Reporting group description:

Participants received TAK-981 90 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months).

| | |
|-----------------------|--|
| Reporting group title | Dose Escalation: TAK-981 60 mg + Pembrolizumab |
|-----------------------|--|

Reporting group description:

Participants received TAK-981 60 mg, IV infusion, on Days 1, 4, 8 and 11 or Days 1 and 8 in each 21-day Treatment Cycle and pembrolizumab 200 mg, IV infusion, as a fixed dose every 3 weeks on Day 1 of 21-day Treatment Cycle until the RP2D was determined (for a maximum of 24 months).

| Serious adverse events | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Expansion: Cohort A: Non- squamous NSCLC TAK-981 120 mg | Dose Expansion: Cohort B: Cervical Cancer |
|---|--|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 9 (44.44%) | 11 / 21 (52.38%) |
| number of deaths (all causes) | 2 | 4 | 9 |
| number of deaths resulting from adverse events | 0 | 0 | 1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (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 |
| Cervix carcinoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colorectal cancer | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infected neoplasm | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-small cell lung cancer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastatic malignant melanoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| 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 disorders | | | |
| Aortic aneurysm rupture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |

| | | | |
|--|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related thrombosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |

| | | | |
|---|---------------|---------------|----------------|
| Anaphylactic shock | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune-mediated lung disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---------------|----------------|----------------|
| Psychiatric disorders | | | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| 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 | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Tracheal obstruction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis radiation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural complication | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transfusion-related acute lung injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic haemothorax | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular block | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| 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 | | | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| 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 | | | |

| | | | |
|---|---------------|---------------|----------------|
| Aplasia pure red cell | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 2 / 21 (9.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea haemorrhagic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| 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 haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal perforation | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| 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 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Biliary obstruction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis acute | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic function abnormal | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant biliary obstruction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatomyositis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| 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 | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| 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 | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| 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 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orchitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 2 / 21 (9.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (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 | | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| 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 | Dose Expansion: Cohort A: Non-squamous NSCLC TAK-981 90 mg | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort F: CPI Refractory Squamous/NSCLC |
|--|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 14 / 28 (50.00%) | 3 / 4 (75.00%) |
| number of deaths (all causes) | 2 | 8 | 1 |
| number of deaths resulting from adverse events | 0 | 2 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervix carcinoma | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colorectal cancer | | | |

| | | | |
|---|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infected neoplasm | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (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 |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-small cell lung cancer | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (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 |
| Metastatic malignant melanoma | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (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 |
| Vascular disorders | | | |
| Aortic aneurysm rupture | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |

| | | | |
|--|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (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 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (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 |
| Device related thrombosis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (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 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |

| | | | |
|---|----------------|----------------|----------------|
| Anaphylactic shock | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 oedema | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (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 |

| | | | |
|---|----------------|----------------|---------------|
| Psychiatric disorders | | | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 | | | |
| Tracheal obstruction | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis radiation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural complication | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transfusion-related acute lung injury | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic haemothorax | | | |

| | | | |
|---|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 28 (7.14%) | 0 / 4 (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 |
| Atrioventricular block | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 | | | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (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 | | | |

| | | | |
|---|----------------|----------------|----------------|
| Aplasia pure red cell | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 28 (7.14%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea haemorrhagic | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 haemorrhage | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal perforation | | | |

| | | | |
|---|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (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 |
| Hepatobiliary disorders | | | |
| Biliary obstruction | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis acute | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic function abnormal | | | |

| | | | |
|---|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant biliary obstruction | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatomyositis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 | | | |
| Myalgia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 / 14 (0.00%) | 0 / 28 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orchitis | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 28 (3.57%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |

| | | | |
|---|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| 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 | | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Dose Expansion: Cohort E: Squamous NSCLC | Dose Expansion: Cohort C: MSS-CRC | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|--|--|--------------------------------------|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 15 (33.33%) | 4 / 9 (44.44%) | 10 / 19 (52.63%) |
| number of deaths (all causes) | 2 | 2 | 4 |
| number of deaths resulting from adverse events | 1 | 1 | 2 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cervix carcinoma | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colorectal cancer | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infected neoplasm | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-small cell lung cancer | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastatic malignant melanoma | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| 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 disorders | | | |
| Aortic aneurysm rupture | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Hypotension | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related thrombosis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |

| | | | |
|---|----------------|---------------|----------------|
| Anaphylactic shock | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| 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 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| 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 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| 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 oedema | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Psychiatric disorders | | | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (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 |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Tracheal obstruction | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis radiation | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural complication | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (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 |
| Transfusion-related acute lung injury | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic haemothorax | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| 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 | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (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 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular block | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (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 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (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 |
| Nervous system disorders | | | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| 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 | | | |

| | | | |
|---|----------------|---------------|----------------|
| Aplasia pure red cell | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea haemorrhagic | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| 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 haemorrhage | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal perforation | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (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 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (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 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| 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 | | | |
| Biliary obstruction | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 2 / 19 (10.53%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis acute | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic function abnormal | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant biliary obstruction | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatomyositis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| 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 | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| 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 | | | |
| Myalgia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| 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 | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orchitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (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 | | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| 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 | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 17 / 33 (51.52%) | 3 / 6 (50.00%) | |
| number of deaths (all causes) | 8 | 2 | |
| number of deaths resulting from adverse events | 4 | 1 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Acute myeloid leukaemia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cancer pain | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervix carcinoma | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colorectal cancer | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Infected neoplasm | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Metastases to central nervous system | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-small cell lung cancer | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastatic malignant melanoma | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Aortic aneurysm rupture | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |

| | | | |
|--|----------------|---------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related thrombosis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |

| | | | |
|---|----------------|---------------|--|
| Anaphylactic shock | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune-mediated lung disease | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|---------------|--|
| Psychiatric disorders | | | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Tracheal obstruction | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis radiation | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural complication | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transfusion-related acute lung injury | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic haemothorax | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Arrhythmia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|----------------|----------------|--|
| Aplasia pure red cell | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea haemorrhagic | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ascites | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 6 (16.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal perforation | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Biliary obstruction | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangitis acute | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic function abnormal | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice cholestatic | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant biliary obstruction | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatomyositis | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orchitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Dose Escalation: TAK-981 40 mg + Pembrolizumab | Dose Expansion: Cohort A: Non- squamous NSCLC TAK-981 120 mg | Dose Expansion: Cohort B: Cervical Cancer |
|---|--|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 9 / 9 (100.00%) | 21 / 21 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Nervous system neoplasm | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour associated fever | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Colon cancer | | | |

| | | | |
|---|--------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Poor peripheral circulation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vasculitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Early satiety | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 9 (33.33%) | 4 / 21 (19.05%) |
| occurrences (all) | 0 | 3 | 5 |
| Chills | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 5 / 9 (55.56%) | 6 / 21 (28.57%) |
| occurrences (all) | 3 | 8 | 6 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site pain | | | |

| | | | |
|---------------------------------------|---------------|----------------|------------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 1 | 3 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 9 (44.44%) | 11 / 21 (52.38%) |
| occurrences (all) | 0 | 19 | 40 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infusion site extravasation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 3 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 2 | 3 |
| Pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 2 |
| Swelling face | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Localised oedema | | | |

| | | | |
|---|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Immune system disorders Cytokine release syndrome subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 21 (4.76%) 2 |
| Reproductive system and breast disorders Epididymal cyst subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Penile oedema subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Perineal pain subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 3 / 21 (14.29%) 3 |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 21 (0.00%) 0 |
| Haemoptysis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 2 / 9 (22.22%) 2 | 1 / 21 (4.76%) 1 |
| Dysphonia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 21 (0.00%) 0 |
| Dyspnoea subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 1 / 9 (11.11%) 2 | 2 / 21 (9.52%) 2 |
| Oropharyngeal pain | | | |

| | | | |
|--------------------------------------|---------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Depression | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 1 | 2 |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 4 / 21 (19.05%) |
| occurrences (all) | 0 | 2 | 10 |
| Aspartate aminotransferase increased | | | |

| | | | |
|---|---------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 9 (44.44%) | 4 / 21 (19.05%) |
| occurrences (all) | 0 | 6 | 11 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 4 / 21 (19.05%) |
| occurrences (all) | 0 | 5 | 9 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| CD4 lymphocytes decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 0 | 3 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |

| | | | |
|---|---------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Electrocardiogram ST-T segment abnormal | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Interleukin level increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 4 / 21 (19.05%) |
| occurrences (all) | 0 | 0 | 10 |
| SARS-CoV-2 test positive | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procalcitonin increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 5 |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| T-lymphocyte count decreased | | | |

| | | | |
|--|--------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 2 / 21 (9.52%) 6 |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 2 / 21 (9.52%) 2 |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 3 / 21 (14.29%) 7 |
| Injury, poisoning and procedural complications | | | |
| Limb injury subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Infusion related reaction subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 21 (4.76%) 13 |
| Oral contusion subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Fall subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Cardiac disorders | | | |
| Angina pectoris subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Sinus tachycardia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 21 (4.76%) 1 |
| Supraventricular tachycardia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Atrial flutter | | | |

| | | | |
|----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Paroxysmal arrhythmia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 2 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 2 |

| | | | |
|--------------------------------------|---------------|----------------|------------------|
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Restless legs syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Tremor | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Parosmia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Polyneuropathy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 13 / 21 (61.90%) |
| occurrences (all) | 0 | 5 | 24 |
| Anaemia of chronic disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Anaemia of malignant disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutropenia | | | |

| | | | |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 10 | 12 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 4 | 4 |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 2 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 6 |
| Lymph node pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Cerumen impaction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diplopia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Visual acuity reduced | | | |

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| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 5 / 21 (23.81%) |
| occurrences (all) | 0 | 1 | 5 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Angular cheilitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 9 (22.22%) | 7 / 21 (33.33%) |
| occurrences (all) | 1 | 4 | 8 |
| Defaecation urgency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 0 | 4 |
| Cheilitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

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| Ascites | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 1 | 2 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intestinal polyp | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 6 / 9 (66.67%) | 9 / 21 (42.86%) |
| occurrences (all) | 1 | 10 | 14 |

| | | | |
|--|---------------------|---------------------|----------------------|
| Mouth ulceration subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 1 / 21 (4.76%) 1 |
| Lip oedema subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Haemorrhoids subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Tongue ulceration subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 2 / 3 (66.67%) 2 | 2 / 9 (22.22%) 2 | 5 / 21 (23.81%) 5 |
| Stomatitis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 2 / 9 (22.22%) 2 | 1 / 21 (4.76%) 1 |
| Hepatobiliary disorders Biliary obstruction subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Cholangitis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Hyperbilirubinaemia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Hypertransaminaemia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Angioedema subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Dermatitis | | | |

| | | | |
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| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 4 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Erythema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis bullous | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis psoriasiform | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ingrowing nail | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Perioral dermatitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

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| Night sweats | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 2 | 3 |
| Rash vesicular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 0 | 9 |
| Rash macular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitiligo | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Chromaturia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cystitis noninfective | | | |

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| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocyturia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 1 | 2 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Dysuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 5 / 21 (23.81%) |
| occurrences (all) | 0 | 0 | 5 |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

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| Musculoskeletal and connective tissue disorders | | | |
| Joint stiffness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 1 / 9 (11.11%) | 4 / 21 (19.05%) |
| occurrences (all) | 2 | 2 | 4 |
| Back pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bone disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 0 | 35 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Polyarthrititis | | | |

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| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 2 |
| Tendon disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Balanitis candida | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dengue fever | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 2 |
| Infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 2 |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
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| Eye infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes simplex reactivation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Kidney infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paronychia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 3 | 5 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Orchitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pulpitis dental | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 9 (11.11%) | 1 / 21 (4.76%) |
| occurrences (all) | 1 | 1 | 2 |

| | | | |
|---|--------------------|---------------------|-----------------------|
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 2 | 1 / 21 (4.76%) 1 |
| Urethritis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 6 / 21 (28.57%) 10 |
| Sinusitis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Skin candida subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Skin infection subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Tinea pedis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Viral infection subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Viral upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 21 (4.76%) 1 |
| Dehydration subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Decreased appetite | | | |

| | | | |
|-----------------------------|---------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 4 / 9 (44.44%) | 4 / 21 (19.05%) |
| occurrences (all) | 0 | 6 | 4 |
| Abnormal weight gain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abnormal loss of weight | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 1 | 4 |
| Hypochloraemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 17 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 3 |
| Steroid diabetes | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyponatraemia | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 1 | 20 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 4 | 3 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 9 (22.22%) | 1 / 21 (4.76%) |
| occurrences (all) | 2 | 5 | 3 |
| Hypoproteinaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| Non-serious adverse events | Dose Expansion: Cohort A: Non- squamous NSCLC TAK-981 90 mg | Dose Expansion: Cohort D: Cutaneous Melanoma | Dose Expansion: Cohort F: CPI Refractory Squamous/NSCLC |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 14 / 14 (100.00%) | 28 / 28 (100.00%) | 4 / 4 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Nervous system neoplasm | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour associated fever | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cancer pain | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 0 | 1 |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |

| | | | |
|--|-----------------|-----------------|----------------|
| Hypotension | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 7 | 2 | 0 |
| Poor peripheral circulation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 3 / 28 (10.71%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Vasculitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Early satiety | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 2 | 2 |
| Chills | | | |
| subjects affected / exposed | 5 / 14 (35.71%) | 4 / 28 (14.29%) | 1 / 4 (25.00%) |
| occurrences (all) | 8 | 6 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 5 / 14 (35.71%) | 9 / 28 (32.14%) | 1 / 4 (25.00%) |
| occurrences (all) | 9 | 12 | 1 |
| Feeling cold | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral swelling | | | |

| | | | |
|---------------------------------------|-----------------|------------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 9 / 14 (64.29%) | 11 / 28 (39.29%) | 1 / 4 (25.00%) |
| occurrences (all) | 21 | 80 | 1 |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Infusion site extravasation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injection site erythema | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Oedema peripheral | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 5 / 28 (17.86%) | 0 / 4 (0.00%) |
| occurrences (all) | 5 | 5 | 0 |
| Pain | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Swelling face | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |

| | | | |
|---|----------------------|------------------------|---------------------|
| Cytokine release syndrome subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 1 / 28 (3.57%) 3 | 0 / 4 (0.00%) 0 |
| Reproductive system and breast disorders | | | |
| Epididymal cyst subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Penile oedema subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Perineal pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 2 / 14 (14.29%) 2 | 10 / 28 (35.71%) 11 | 0 / 4 (0.00%) 0 |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 4 (0.00%) 0 |
| Haemoptysis subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Dysphonia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Dyspnoea subjects affected / exposed occurrences (all) | 2 / 14 (14.29%) 2 | 1 / 28 (3.57%) 1 | 2 / 4 (50.00%) 2 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 28 (3.57%) 2 | 0 / 4 (0.00%) 0 |
| Rhinorrhoea | | | |

| | | | |
|--|----------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 4 (0.00%) 0 |
| Productive cough subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 2 / 28 (7.14%) 2 | 0 / 4 (0.00%) 0 |
| Pleural effusion subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Psychiatric disorders | | | |
| Agitation subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Anxiety subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 2 / 28 (7.14%) 2 | 0 / 4 (0.00%) 0 |
| Depression subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 2 / 28 (7.14%) 2 | 0 / 4 (0.00%) 0 |
| Hallucination subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Insomnia subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 1 / 28 (3.57%) 1 | 0 / 4 (0.00%) 0 |
| Libido decreased subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Investigations | | | |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 2 / 14 (14.29%) 3 | 1 / 28 (3.57%) 1 | 0 / 4 (0.00%) 0 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 4 / 14 (28.57%) 9 | 3 / 28 (10.71%) 3 | 0 / 4 (0.00%) 0 |
| Alanine aminotransferase increased | | | |

| | | | |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed | 4 / 14 (28.57%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 5 | 3 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 28 (3.57%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 1 | 2 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CD4 lymphocytes decreased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 5 / 28 (17.86%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 8 | 0 |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 2 / 4 (50.00%) |
| occurrences (all) | 0 | 1 | 3 |
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Electrocardiogram ST-T segment abnormal | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Interleukin level increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 3 / 28 (10.71%) | 0 / 4 (0.00%) |
| occurrences (all) | 7 | 5 | 0 |
| SARS-CoV-2 test positive | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Procalcitonin increased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 4 | 3 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| T-lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Limb injury | | | |
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Infusion related reaction | | | |
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 4 (0.00%) 0 |
| Oral contusion | | | |
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 1 / 28 (3.57%) 1 | 0 / 4 (0.00%) 0 |
| Fall | | | |
| subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 1 / 28 (3.57%) 1 | 0 / 4 (0.00%) 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 4 | 1 / 28 (3.57%) 1 | 0 / 4 (0.00%) 0 |
| Atrial flutter | | | |
| subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Cardiac failure | | | |

| | | | |
|----------------------------------|-----------------|-----------------|---------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paroxysmal arrhythmia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| Balance disorder | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Headache | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 5 / 28 (17.86%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 12 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

| | | | |
|--------------------------------------|-----------------|-----------------|----------------|
| Burning sensation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Restless legs syndrome | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Parosmia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Polyneuropathy | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 7 / 28 (25.00%) | 2 / 4 (50.00%) |
| occurrences (all) | 5 | 9 | 7 |
| Anaemia of chronic disease | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anaemia of malignant disease | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 4 / 14 (28.57%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 8 | 3 | 0 |
| Thrombocytopenia | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 2 / 14 (14.29%) | 2 / 28 (7.14%) | 1 / 4 (25.00%) |
| occurrences (all) | 8 | 4 | 1 |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Lymph node pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Cerumen impaction | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diplopia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Visual acuity reduced | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ocular hyperaemia | | | |

| | | | |
|--|---------------------|---------------------|--------------------|
| subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Angular cheilitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 7 / 28 (25.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 3 | 17 | 1 |
| Defaecation urgency | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cheilitis | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-------------------------------|-----------------|------------------|----------------|
| Flatulence | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intestinal polyp | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Odynophagia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Nausea | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 13 / 28 (46.43%) | 1 / 4 (25.00%) |
| occurrences (all) | 6 | 40 | 1 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|----------------------|-----------------------|---------------------|
| Lip oedema subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Haemorrhoids subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Tongue ulceration subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 1 / 4 (25.00%) 1 |
| Vomiting subjects affected / exposed occurrences (all) | 4 / 14 (28.57%) 5 | 4 / 28 (14.29%) 19 | 1 / 4 (25.00%) 6 |
| Stomatitis subjects affected / exposed occurrences (all) | 4 / 14 (28.57%) 4 | 8 / 28 (28.57%) 16 | 0 / 4 (0.00%) 0 |
| Hepatobiliary disorders Biliary obstruction subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Cholangitis subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Hyperbilirubinaemia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Hypertransaminaemia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Angioedema subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Dermatitis subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Dermatitis acneiform | | | |

| | | | |
|---|----------------|-----------------|---------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 4 / 28 (14.29%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 7 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Erythema | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis bullous | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis psoriasiform | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ingrowing nail | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Perioral dermatitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

| | | | |
|-----------------------------|----------------|-----------------|---------------|
| Psoriasis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 6 / 28 (21.43%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 9 | 0 |
| Rash vesicular | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 3 / 28 (10.71%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 6 | 0 |
| Rash macular | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitiligo | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 7 / 28 (25.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 10 | 0 |
| Renal and urinary disorders | | | |
| Chromaturia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cystitis noninfective | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Leukocyturia | | | |

| | | | |
|---|-----------------|----------------|---------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dysuria | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------|-----------------|-----------------|---------------|
| Joint stiffness | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bone pain | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Arthralgia | | | |
| subjects affected / exposed | 4 / 14 (28.57%) | 5 / 28 (17.86%) | 0 / 4 (0.00%) |
| occurrences (all) | 13 | 5 | 0 |
| Back pain | | | |
| subjects affected / exposed | 3 / 14 (21.43%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Bone disorder | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 5 / 28 (17.86%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 9 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Polyarthrititis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|----------------------|---------------------|---------------------|
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 2 / 28 (7.14%) 2 | 1 / 4 (25.00%) 1 |
| Osteoarthritis subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 2 / 28 (7.14%) 2 | 0 / 4 (0.00%) 0 |
| Spinal pain subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Tendon disorder subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Infections and infestations | | | |
| Balanitis candida subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 1 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| COVID-19 subjects affected / exposed occurrences (all) | 3 / 14 (21.43%) 3 | 2 / 28 (7.14%) 2 | 0 / 4 (0.00%) 0 |
| Dengue fever subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 2 / 28 (7.14%) 2 | 0 / 4 (0.00%) 0 |
| Gastrointestinal infection subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Influenza subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 2 / 28 (7.14%) 2 | 0 / 4 (0.00%) 0 |
| Infection subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Gastroenteritis norovirus subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Eye infection | | | |

| | | | |
|-----------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes simplex reactivation | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Kidney infection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paronychia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 0 / 28 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 2 | 0 | 2 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Orchitis | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pulpitis dental | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 28 (7.14%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 2 | 2 |
| Upper respiratory tract infection | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 14 (7.14%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Urethritis | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 5 / 28 (17.86%) | 0 / 4 (0.00%) |
| occurrences (all) | 3 | 7 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin candida | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tinea pedis | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 5 / 28 (17.86%) | 3 / 4 (75.00%) |
| occurrences (all) | 1 | 6 | 4 |

| | | | |
|-----------------------------|-----------------|-----------------|----------------|
| Abnormal weight gain | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Abnormal loss of weight | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 3 / 28 (10.71%) | 1 / 4 (25.00%) |
| occurrences (all) | 1 | 3 | 1 |
| Hypochloraemia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 3 / 28 (10.71%) | 3 / 4 (75.00%) |
| occurrences (all) | 9 | 3 | 3 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 2 / 14 (14.29%) | 2 / 28 (7.14%) | 0 / 4 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Steroid diabetes | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 14 (0.00%) | 0 / 28 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 14 (7.14%) | 1 / 28 (3.57%) | 0 / 4 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |

| | | | |
|--|---------------------|---------------------|--------------------|
| Hypomagnesaemia subjects affected / exposed occurrences (all) | 1 / 14 (7.14%) 2 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Hypokalaemia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Hypoproteinaemia subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |
| Type 2 diabetes mellitus subjects affected / exposed occurrences (all) | 0 / 14 (0.00%) 0 | 0 / 28 (0.00%) 0 | 0 / 4 (0.00%) 0 |

| Non-serious adverse events | Dose Expansion: Cohort E: Squamous NSCLC | Dose Expansion: Cohort C: MSS-CRC | Dose Escalation: TAK-981 120 mg + Pembrolizumab |
|---|--|--------------------------------------|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 14 / 15 (93.33%) | 9 / 9 (100.00%) | 19 / 19 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Nervous system neoplasm subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 19 (0.00%) 0 |
| Tumour associated fever subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 2 |
| Tumour pain subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 9 (11.11%) 1 | 1 / 19 (5.26%) 1 |
| Cancer pain subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 2 / 9 (22.22%) 3 | 1 / 19 (5.26%) 1 |
| Colon cancer subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Vascular disorders Hypotension subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 9 (11.11%) 3 | 2 / 19 (10.53%) 3 |

| | | | |
|---|----------------------|---------------------|------------------------|
| Poor peripheral circulation subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 2 |
| Hot flush subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Hypertension subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Vasculitis subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Early satiety subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 19 (0.00%) 0 |
| Asthenia subjects affected / exposed occurrences (all) | 3 / 15 (20.00%) 3 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Chills subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 1 / 9 (11.11%) 1 | 11 / 19 (57.89%) 20 |
| Fatigue subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 5 / 9 (55.56%) 8 | 4 / 19 (21.05%) 9 |
| Feeling cold subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Injection site pain subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Peripheral swelling subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Pyrexia | | | |

| | | | |
|---------------------------------------|-----------------|----------------|------------------|
| subjects affected / exposed | 6 / 15 (40.00%) | 3 / 9 (33.33%) | 14 / 19 (73.68%) |
| occurrences (all) | 22 | 4 | 59 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 3 / 19 (15.79%) |
| occurrences (all) | 0 | 0 | 5 |
| Infusion site extravasation | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 3 / 19 (15.79%) |
| occurrences (all) | 0 | 0 | 5 |
| Pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Swelling face | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 2 |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Immune system disorders | | | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 1 | 0 | 8 |

| | | | |
|---|----------------|----------------|-----------------|
| Reproductive system and breast disorders | | | |
| Epididymal cyst | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Penile oedema | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Perineal pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 2 / 9 (22.22%) | 4 / 19 (21.05%) |
| occurrences (all) | 0 | 2 | 4 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 2 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 4 / 19 (21.05%) |
| occurrences (all) | 0 | 1 | 6 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Productive cough | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Pleural effusion subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Psychiatric disorders | | | |
| Agitation subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Anxiety subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 19 (0.00%) 0 |
| Depression subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 19 (0.00%) 0 |
| Hallucination subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 19 (0.00%) 0 |
| Insomnia subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 1 / 9 (11.11%) 1 | 0 / 19 (0.00%) 0 |
| Libido decreased subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Investigations | | | |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 1 / 9 (11.11%) 1 | 0 / 19 (0.00%) 0 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 2 | 2 / 9 (22.22%) 3 | 2 / 19 (10.53%) 2 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Blood bilirubin increased | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| CD4 lymphocytes decreased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood pressure increased | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Electrocardiogram ST-T segment abnormal | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |

| | | | |
|--|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Interleukin level increased | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 9 | 0 | 1 |
| SARS-CoV-2 test positive | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Procalcitonin increased | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 3 / 19 (15.79%) |
| occurrences (all) | 1 | 0 | 7 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| T-lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 2 / 19 (10.53%) |
| occurrences (all) | 0 | 2 | 4 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|----------------|----------------|-----------------|
| Injury, poisoning and procedural complications | | | |
| Limb injury | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all) | 0 | 0 | 4 |
| Oral contusion | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 2 |
| Fall | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 2 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all) | 1 | 0 | 2 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 1 | 2 |
| Pericardial effusion | | | |

| | | | |
|----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paroxysmal arrhythmia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 2 / 9 (22.22%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 2 | 1 |
| Headache | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 2 / 9 (22.22%) | 4 / 19 (21.05%) |
| occurrences (all) | 0 | 4 | 4 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Restless legs syndrome | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--------------------------------------|-----------------|----------------|-----------------|
| Seizure | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 1 | 1 |
| Parosmia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Polyneuropathy | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 3 / 9 (33.33%) | 6 / 19 (31.58%) |
| occurrences (all) | 2 | 8 | 7 |
| Anaemia of chronic disease | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anaemia of malignant disease | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 9 (11.11%) | 4 / 19 (21.05%) |
| occurrences (all) | 1 | 1 | 18 |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocytosis | | | |

| | | | |
|--|---------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Leukopenia subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Lymph node pain subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Ear and labyrinth disorders Cerumen impaction subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Vertigo subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Tinnitus subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Eye disorders Dry eye subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Diplopia subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Visual acuity reduced subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Ocular hyperaemia subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Abdominal pain lower | | | |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 3 / 9 (33.33%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 4 | 1 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 2 / 9 (22.22%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Angular cheilitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 15 (20.00%) | 3 / 9 (33.33%) | 9 / 19 (47.37%) |
| occurrences (all) | 5 | 4 | 12 |
| Defaecation urgency | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Constipation | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 1 | 1 |
| Cheilitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 1 | 1 |
| Dry mouth | | | |

| | | | |
|-------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Intestinal polyp | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 2 / 9 (22.22%) | 5 / 19 (26.32%) |
| occurrences (all) | 1 | 2 | 5 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lip oedema | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all) | 0 | 0 | 2 |
| Tongue ulceration | | | |

| | | | |
|--|---------------------|---------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 2 / 9 (22.22%) 2 | 5 / 19 (26.32%) 6 |
| Stomatitis subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 5 | 3 / 9 (33.33%) 4 | 8 / 19 (42.11%) 11 |
| Hepatobiliary disorders Biliary obstruction subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Cholangitis subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Hyperbilirubinaemia subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 3 |
| Hypertransaminasaemia subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Angioedema subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Dermatitis subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Dermatitis acneiform subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 2 / 19 (10.53%) 2 |
| Alopecia subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Erythema | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis bullous | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis psoriasiform | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 2 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ingrowing nail | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Perioral dermatitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palmar-plantar erythrodysesthesia syndrome | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 2 / 19 (10.53%) |
| occurrences (all) | 0 | 0 | 2 |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 1 | 0 | 1 |

| | | | |
|---|---------------------|--------------------|----------------------|
| Rash erythematous subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Pruritus subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 3 / 19 (15.79%) 4 |
| Rash vesicular subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 4 / 19 (21.05%) 6 |
| Rash macular subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Urticaria subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 2 |
| Vitiligo subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Chromaturia subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Cystitis noninfective subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Leukocyturia subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Proteinuria subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Haematuria | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Dysuria subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Hydronephrosis subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 19 (0.00%) 0 |
| Renal impairment subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Urinary retention subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Urinary incontinence subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Adrenal insufficiency subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 19 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Joint stiffness subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Bone pain subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Arthralgia | | | |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 15 (6.67%) | 2 / 9 (22.22%) | 3 / 19 (15.79%) |
| occurrences (all) | 1 | 2 | 6 |
| Back pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Bone disorder | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 1 | 1 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Polyarthritis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal pain | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Tendon disorder subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Infections and infestations | | | |
| Balanitis candida subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| COVID-19 subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 19 (0.00%) 0 |
| Dengue fever subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Gastrointestinal infection subjects affected / exposed occurrences (all) | 1 / 15 (6.67%) 1 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Influenza subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Infection subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 19 (0.00%) 0 |
| Gastroenteritis norovirus subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Eye infection subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Herpes simplex reactivation subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 19 (5.26%) 1 |
| Herpes zoster subjects affected / exposed occurrences (all) | 0 / 15 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 19 (0.00%) 0 |

| | | | |
|-----------------------------------|----------------|----------------|-----------------|
| Kidney infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Paronychia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 3 / 19 (15.79%) |
| occurrences (all) | 0 | 1 | 3 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Orchitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulpitis dental | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 1 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urethritis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 1 | 1 |

| | | | |
|---|----------------|----------------|-----------------|
| Sinusitis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin candida | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinea pedis | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 2 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 2 | 2 |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 3 / 9 (33.33%) | 6 / 19 (31.58%) |
| occurrences (all) | 1 | 4 | 7 |
| Abnormal weight gain | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abnormal loss of weight | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 1 | 1 |
| Hypochloraemia | | | |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 2 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 0 | 1 |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Steroid diabetes | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 15 (6.67%) | 1 / 9 (11.11%) | 0 / 19 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 1 / 9 (11.11%) | 1 / 19 (5.26%) |
| occurrences (all) | 0 | 1 | 1 |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 15 (13.33%) | 1 / 9 (11.11%) | 5 / 19 (26.32%) |
| occurrences (all) | 4 | 2 | 7 |
| Hypoproteinaemia | | | |

| | | | |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 15 (0.00%) | 0 / 9 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Dose Escalation: TAK-981 90 mg + Pembrolizumab | Dose Escalation: TAK-981 60 mg + Pembrolizumab | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 33 / 33 (100.00%) | 6 / 6 (100.00%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Nervous system neoplasm | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tumour associated fever | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Colon cancer | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Poor peripheral circulation | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hot flush | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypertension | | | |

| | | | |
|--|------------------|----------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vasculitis | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| General disorders and administration site conditions | | | |
| Early satiety | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Asthenia | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Chills | | | |
| subjects affected / exposed | 12 / 33 (36.36%) | 1 / 6 (16.67%) | |
| occurrences (all) | 27 | 1 | |
| Fatigue | | | |
| subjects affected / exposed | 13 / 33 (39.39%) | 1 / 6 (16.67%) | |
| occurrences (all) | 15 | 1 | |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Injection site pain | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 17 / 33 (51.52%) | 1 / 6 (16.67%) | |
| occurrences (all) | 37 | 5 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Influenza like illness | | | |

| | | | |
|--|-----------------|----------------|--|
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infusion site extravasation | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Injection site erythema | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Pain | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Malaise | | | |
| subjects affected / exposed | 4 / 33 (12.12%) | 0 / 6 (0.00%) | |
| occurrences (all) | 7 | 0 | |
| Swelling face | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Immune system disorders | | | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 0 / 6 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Reproductive system and breast disorders | | | |
| Epididymal cyst | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Penile oedema | | | |

| | | | |
|---|-----------------|---------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Perineal pain | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dysphonia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 5 / 33 (15.15%) | 0 / 6 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Productive cough | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pleural effusion | | | |

| | | | |
|--|---------------------|--------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Depression | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hallucination | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Insomnia | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Libido decreased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Investigations | | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 5 / 33 (15.15%) | 0 / 6 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 13 / 33 (39.39%) | 0 / 6 (0.00%) | |
| occurrences (all) | 17 | 0 | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 7 / 33 (21.21%) | 0 / 6 (0.00%) | |
| occurrences (all) | 8 | 0 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Blood creatinine increased | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 3 / 33 (9.09%) | 0 / 6 (0.00%) | |
| occurrences (all) | 7 | 0 | |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| CD4 lymphocytes decreased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Blood pressure increased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Electrocardiogram ST-T segment abnormal | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Interleukin level increased | | | |

| | | | |
|--|-----------------|---------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| SARS-CoV-2 test positive | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Procalcitonin increased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 6 / 33 (18.18%) | 0 / 6 (0.00%) | |
| occurrences (all) | 14 | 0 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| N-terminal prohormone brain natriuretic peptide increased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| T-lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Weight decreased | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|------------------------------|-----------------|---------------|--|
| Limb injury | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Infusion related reaction | | | |
| subjects affected / exposed | 7 / 33 (21.21%) | 0 / 6 (0.00%) | |
| occurrences (all) | 19 | 0 | |
| Oral contusion | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Fall | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Palpitations | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pericardial effusion | | | |

| | | | |
|----------------------------------|-----------------|----------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Paroxysmal arrhythmia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nervous system disorders | | | |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dysgeusia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Headache | | | |
| subjects affected / exposed | 6 / 33 (18.18%) | 1 / 6 (16.67%) | |
| occurrences (all) | 7 | 1 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Burning sensation | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 2 | |
| Restless legs syndrome | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|--------------------------------------|------------------|----------------|--|
| Seizure | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Somnolence | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tremor | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Parosmia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Polyneuropathy | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 16 / 33 (48.48%) | 1 / 6 (16.67%) | |
| occurrences (all) | 32 | 3 | |
| Anaemia of chronic disease | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Anaemia of malignant disease | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Leukocytosis | | | |

| | | | |
|--|---------------------|--------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Leukopenia subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Lymph node pain subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Ear and labyrinth disorders Cerumen impaction subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Vertigo subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Tinnitus subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Eye disorders Dry eye subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Diplopia subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Visual acuity reduced subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Ocular hyperaemia subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) | 2 / 33 (6.06%) 2 | 0 / 6 (0.00%) 0 | |
| Abdominal pain lower | | | |

| | | |
|-----------------------------|-----------------|----------------|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Abdominal pain | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 |
| Abdominal distension | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 |
| Anal fissure | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 |
| Angular cheilitis | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Diarrhoea | | |
| subjects affected / exposed | 9 / 33 (27.27%) | 0 / 6 (0.00%) |
| occurrences (all) | 16 | 0 |
| Defaecation urgency | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Constipation | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 1 |
| Cheilitis | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Ascites | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 |
| Flatulence | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Dyspepsia | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 1 |
| Dry mouth | | |

| | | | |
|-------------------------------|-----------------|---------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Intestinal polyp | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 8 / 33 (24.24%) | 0 / 6 (0.00%) | |
| occurrences (all) | 10 | 0 | |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Lip oedema | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tongue ulceration | | | |

| | | | |
|--|-----------------|---------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 7 / 33 (21.21%) | 0 / 6 (0.00%) | |
| occurrences (all) | 7 | 0 | |
| Stomatitis | | | |
| subjects affected / exposed | 8 / 33 (24.24%) | 0 / 6 (0.00%) | |
| occurrences (all) | 13 | 0 | |
| Hepatobiliary disorders | | | |
| Biliary obstruction | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Erythema | | | |

| | | | |
|---|----------------|---------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dermatitis bullous | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dry skin | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dermatitis psoriasiform | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Ingrowing nail | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Rash | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Perioral dermatitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Palmar-plantar erythrodysesthesia syndrome | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Night sweats | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Psoriasis | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |

| | | | |
|---|---------------------|---------------------|--|
| Rash erythematous subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Pruritus subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Rash vesicular subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 2 / 33 (6.06%) 4 | 0 / 6 (0.00%) 0 | |
| Rash macular subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 1 / 6 (16.67%) 1 | |
| Urticaria subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 1 / 6 (16.67%) 1 | |
| Vitiligo subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Renal and urinary disorders | | | |
| Chromaturia subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Cystitis noninfective subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Leukocyturia subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Proteinuria subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 | 0 / 6 (0.00%) 0 | |
| Haematuria | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Urinary incontinence | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypothyroidism | | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Joint stiffness | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Bone pain | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Arthralgia | | | |

| | | |
|-----------------------------|-----------------|----------------|
| subjects affected / exposed | 5 / 33 (15.15%) | 2 / 6 (33.33%) |
| occurrences (all) | 5 | 2 |
| Back pain | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 1 / 6 (16.67%) |
| occurrences (all) | 4 | 1 |
| Bone disorder | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Myalgia | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 0 |
| Musculoskeletal stiffness | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Musculoskeletal pain | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Musculoskeletal chest pain | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Neck pain | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 |
| Muscular weakness | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 1 |
| Polyarthritis | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Pain in extremity | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 0 |
| Osteoarthritis | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Spinal pain | | |

| | | | |
|---|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Tendon disorder subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Infections and infestations | | | |
| Balanitis candida subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| COVID-19 subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 | 1 / 6 (16.67%) 1 | |
| Dengue fever subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Gastrointestinal infection subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Influenza subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Infection subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Gastroenteritis norovirus subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 1 / 6 (16.67%) 1 | |
| Eye infection subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |
| Herpes simplex reactivation subjects affected / exposed occurrences (all) | 1 / 33 (3.03%) 1 | 0 / 6 (0.00%) 0 | |
| Herpes zoster subjects affected / exposed occurrences (all) | 0 / 33 (0.00%) 0 | 0 / 6 (0.00%) 0 | |

| | | |
|-----------------------------------|-----------------|---------------|
| Kidney infection | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Paronychia | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Oral herpes | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 |
| Oral candidiasis | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Nasopharyngitis | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 |
| Orchitis | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Respiratory tract infection | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Pulpitis dental | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Pneumonia | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 |
| Upper respiratory tract infection | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Urethritis | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Urinary tract infection | | |
| subjects affected / exposed | 4 / 33 (12.12%) | 0 / 6 (0.00%) |
| occurrences (all) | 5 | 0 |

| | | | |
|---|------------------|----------------|--|
| Sinusitis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin candida | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Skin infection | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Tinea pedis | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 1 / 6 (16.67%) | |
| occurrences (all) | 1 | 1 | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 1 / 6 (16.67%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Decreased appetite | | | |
| subjects affected / exposed | 10 / 33 (30.30%) | 0 / 6 (0.00%) | |
| occurrences (all) | 12 | 0 | |
| Abnormal weight gain | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Abnormal loss of weight | | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypochloraemia | | | |

| | | |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Hypocalcaemia | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Hypoalbuminaemia | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 |
| Hyperuricaemia | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Hyperphosphataemia | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Hypertriglyceridaemia | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Hyperglycaemia | | |
| subjects affected / exposed | 1 / 33 (3.03%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 |
| Steroid diabetes | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 |
| Hypophosphataemia | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 |
| Hyponatraemia | | |
| subjects affected / exposed | 2 / 33 (6.06%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 0 |
| Hypomagnesaemia | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 1 / 6 (16.67%) |
| occurrences (all) | 4 | 1 |
| Hypokalaemia | | |
| subjects affected / exposed | 3 / 33 (9.09%) | 1 / 6 (16.67%) |
| occurrences (all) | 4 | 1 |
| Hypoproteinaemia | | |

| | | | |
|-----------------------------|----------------|---------------|--|
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 33 (0.00%) | 0 / 6 (0.00%) | |
| occurrences (all) | 0 | 0 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 22 April 2020 | The following changes were made as per amendment 01: 1. Modified inclusion and exclusion criteria. 2. Added a 90-day follow-up visit after last dose with the study treatment to capture any late-onset immune-related AEs. 3. Added AESI definition, procedure for recording and reporting AESIs, and monitoring of AESIs. |
| 10 February 2021 | The following changes were made as per amendment 02: 1. Modified inclusion criteria. 2. Added DCR, DRR, TTP, and OS as secondary endpoints for disclosure for phase 2. |
| 23 April 2021 | The following changes were made as per amendment 03: 1. Incorporated additional local laboratory assessments for safety during Cycle 1. 2. Provided guidance on COVID-19 vaccination and procedures during the trial. |
| 09 September 2021 | The primary reason for amendment 04 was to update the translational strategy for sample collection for analysis of biomarkers in phase 2. |
| 01 July 2022 | The primary reason for amendment 05 was to expand phase 2 enrollment in Cohort A to evaluate the dose regimen of subasumstat at 120 mg QW in addition to the 90 mg BIW dose regimen. |
| 22 June 2023 | The primary reason for amendment 06 was to remove nonsquamous NSCLC, SCLC, and MSI-H/dMMR CRC populations. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported