

**Clinical trial results:****A Phase 1/2, Open-label Study to Evaluate the Safety and Antitumor Activity of MEDI0680 (AMP-514) in Combination with Durvalumab versus Nivolumab Monotherapy in Subjects with Select Advanced Malignancies
Summary**

| | |
|--------------------------|----------------|
| EudraCT number | 2016-000323-43 |
| Trial protocol | GB NL |
| Global end of trial date | 17 March 2020 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v2 (current) |
| This version publication date | 26 May 2021 |
| First version publication date | 20 March 2021 |
| Version creation reason | |

Trial information**Trial identification**

| | |
|-----------------------|-------------|
| Sponsor protocol code | D6020C00001 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02118337 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | MedImmune, LLC |
| Sponsor organisation address | One MedImmune Way, Gaithersburg, United States, 20878 |
| Public contact | Farzana Walcott, MedImmune, LLC, +1 3013983063, information.center@astrazeneca.com |
| Scientific contact | Farzana Walcott, MedImmune, LLC, +1 3013983063, information.center@astrazeneca.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 30 October 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 March 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objectives of the study are as below:

1. For dose-escalation phase: To determine safety profile of of MEDI0680 in combination with durvalumab in participants with select advanced malignancies.
2. For dose-expansion: To evaluate the antitumor activity of MEDI0680 in combination with durvalumab versus nivolumab monotherapy in immunotherapy naïve participants with advanced or metastatic clear cell renal cell carcinoma (ccRCC) as based on investigator assessed response using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Participants signed an informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 19 May 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Australia: 7 |
| Country: Number of subjects enrolled | Canada: 5 |
| Country: Number of subjects enrolled | France: 8 |
| Country: Number of subjects enrolled | Netherlands: 8 |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Country: Number of subjects enrolled | United States: 66 |
| Worldwide total number of subjects | 97 |
| EEA total number of subjects | 16 |

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) | 56 |
| From 65 to 84 years | 40 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

The study is conducted in Australia, Canada, France, Netherlands, United Kingdom, and the United States.

Pre-assignment

Screening details:

Of the 130 participants screened, 97 participants were enrolled and were treated in this study.

Period 1

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

Arms

| | |
|------------------------------|--------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | MEDI0680 0.1 mg/kg + Durvalumab 3 mg |

Arm description:

Participants in dose-escalation phase received IV infusion of MEDI0680 0.1 mg/kg and durvalumab 3 mg/kg every 2 weeks (Q2W) for up to 12 months.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | MEDI0680 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Intravenous (IV) infusion of MEDI0680 0.1 mg/kg Q2W for up to 12 months.

| | |
|--|--|
| Investigational medicinal product name | Durvalumab |
| Investigational medicinal product code | MEDI4736 |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of durvalumab 3 mg Q2W for up to 12 months.

| | |
|------------------|---------------------------------------|
| Arm title | MEDI0680 0.1 mg/kg + Durvalumab 10 mg |
|------------------|---------------------------------------|

Arm description:

Participants in dose-escalation phase received IV infusion of MEDI0680 0.1 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | MEDI0680 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of MEDI0680 0.1 mg/kg Q2W for up to 12 months.

| | |
|--|--|
| Investigational medicinal product name | Durvalumab |
| Investigational medicinal product code | MEDI4736 |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| IV infusion of durvalumab 10 mg Q2W for up to 12 months. | |
| Arm title | MEDI0680 0.5 mg/kg + Durvalumab 10 mg |

Arm description:

Participants in dose-escalation phase received IV infusion of MEDI0680 0.5 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | MEDI0680 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of MEDI0680 0.5 mg/kg Q2W for up to 12 months.

| | |
|--|--|
| Investigational medicinal product name | Durvalumab |
| Investigational medicinal product code | MEDI4736 |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of durvalumab 10 mg Q2W for up to 12 months.

| | |
|------------------|---------------------------------------|
| Arm title | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|------------------|---------------------------------------|

Arm description:

Participants in dose-escalation phase received IV infusion of MEDI0680 2.5 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | MEDI0680 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of MEDI0680 2.5 mg/kg Q2W for up to 12 months.

| | |
|--|--|
| Investigational medicinal product name | Durvalumab |
| Investigational medicinal product code | MEDI4736 |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of durvalumab 10 mg Q2W for up to 12 months.

| | |
|------------------|--------------------------------------|
| Arm title | MEDI0680 10 mg/kg + Durvalumab 10 mg |
|------------------|--------------------------------------|

Arm description:

Participants in dose-escalation phase received IV infusion of MEDI0680 10 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months.

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

| | |
|--|-----------------------|
| Investigational medicinal product name | MEDI0680 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of MEDI0680 10 mg/kg Q2W for up to 12 months.

| | |
|--|--|
| Investigational medicinal product name | Durvalumab |
| Investigational medicinal product code | MEDI4736 |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of durvalumab 10 mg Q2W for up to 12 months.

| | |
|------------------|--------------------------------------|
| Arm title | MEDI0680 20 mg/kg + Durvalumab 10 mg |
|------------------|--------------------------------------|

Arm description:

Participants in dose-escalation phase received IV infusion of MEDI0680 20 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | MEDI0680 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of MEDI0680 20 mg/kg Q2W for up to 12 months

| | |
|--|--|
| Investigational medicinal product name | Durvalumab |
| Investigational medicinal product code | MEDI4736 |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of durvalumab 10 mg Q2W for up to 12 months.

| | |
|------------------|-------------------|
| Arm title | MEDI0680 20 mg/kg |
|------------------|-------------------|

Arm description:

Participants in dose-expansion phase received IV infusion of MEDI0680 20 mg/kg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | MEDI0680 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of MEDI0680 20 mg/kg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first.

| | |
|------------------|---------------------------------------|
| Arm title | MEDI0680 20 mg/kg + Durvalumab 750 mg |
|------------------|---------------------------------------|

Arm description:

Participants in dose-expansion phase received IV infusion of MEDI0680 20 mg/kg and durvalumab 750 mg/kg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | MEDI0680 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of MEDI0680 20 mg/kg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first.

| | |
|--|--|
| Investigational medicinal product name | Durvalumab |
| Investigational medicinal product code | MEDI4736 |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

IV infusion of durvalumab 750 mg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first.

| | |
|------------------|------------------|
| Arm title | Nivolumab 240 mg |
|------------------|------------------|

Arm description:

Participants in dose-expansion phase received IV infusion of nivolumab 240 mg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first.

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

Dosage and administration details:

IV infusion of nivolumab 240 mg/kg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first.

| Number of subjects in period 1 | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg |
|---------------------------------------|--------------------------------------|---------------------------------------|---------------------------------------|
| Started | 4 | 5 | 3 |
| Completed | 0 | 0 | 0 |
| Not completed | 4 | 5 | 3 |
| Consent withdrawn by subject | 1 | 3 | 2 |
| Death | 2 | 2 | 1 |
| Unspecified | 1 | - | - |
| Lost to follow-up | - | - | - |

| Number of subjects in period 1 | MEDI0680 2.5 mg/kg + Durvalumab 10 mg | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg |
|---------------------------------------|---------------------------------------|--------------------------------------|--------------------------------------|
| Started | 3 | 9 | 6 |

| | | | |
|------------------------------|---|---|---|
| Completed | 0 | 0 | 0 |
| Not completed | 3 | 9 | 6 |
| Consent withdrawn by subject | 1 | 2 | 2 |
| Death | 2 | 5 | 1 |
| Unspecified | - | 2 | 3 |
| Lost to follow-up | - | - | - |

| Number of subjects in period 1 | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg |
|--------------------------------|-------------------|---|------------------|
| | | | |
| Started | 4 | 42 | 21 |
| Completed | 0 | 0 | 0 |
| Not completed | 4 | 42 | 21 |
| Consent withdrawn by subject | 1 | 4 | 2 |
| Death | 2 | 9 | 4 |
| Unspecified | 1 | 28 | 15 |
| Lost to follow-up | - | 1 | - |

Baseline characteristics

Reporting groups

| | |
|---|---------------------------------------|
| Reporting group title | MEDI0680 0.1 mg/kg + Durvalumab 3 mg |
| Reporting group description: Participants in dose-escalation phase received IV infusion of MEDI0680 0.1 mg/kg and durvalumab 3 mg/kg every 2 weeks (Q2W) for up to 12 months. | |
| Reporting group title | MEDI0680 0.1 mg/kg + Durvalumab 10 mg |
| Reporting group description: Participants in dose-escalation phase received IV infusion of MEDI0680 0.1 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months. | |
| Reporting group title | MEDI0680 0.5 mg/kg + Durvalumab 10 mg |
| Reporting group description: Participants in dose-escalation phase received IV infusion of MEDI0680 0.5 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months. | |
| Reporting group title | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
| Reporting group description: Participants in dose-escalation phase received IV infusion of MEDI0680 2.5 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months. | |
| Reporting group title | MEDI0680 10 mg/kg + Durvalumab 10 mg |
| Reporting group description: Participants in dose-escalation phase received IV infusion of MEDI0680 10 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months. | |
| Reporting group title | MEDI0680 20 mg/kg + Durvalumab 10 mg |
| Reporting group description: Participants in dose-escalation phase received IV infusion of MEDI0680 20 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months. | |
| Reporting group title | MEDI0680 20 mg/kg |
| Reporting group description: Participants in dose-expansion phase received IV infusion of MEDI0680 20 mg/kg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first. | |
| Reporting group title | MEDI0680 20 mg/kg + Durvalumab 750 mg |
| Reporting group description: Participants in dose-expansion phase received IV infusion of MEDI0680 20 mg/kg and durvalumab 750 mg/kg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first. | |
| Reporting group title | Nivolumab 240 mg |
| Reporting group description: Participants in dose-expansion phase received IV infusion of nivolumab 240 mg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first. | |

| Reporting group values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg |
|--|--------------------------------------|---------------------------------------|---------------------------------------|
| Number of subjects | 4 | 5 | 3 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |

| | | | |
|---|--------|-------|--------|
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 2 | 2 | 2 |
| From 65-84 years | 2 | 3 | 1 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 60.5 | 67.4 | 52.3 |
| standard deviation | ± 12.6 | ± 8.4 | ± 17.9 |
| Sex: Female, Male Units: Participants | | | |
| Female | 1 | 3 | 1 |
| Male | 3 | 2 | 2 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 1 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 0 |
| White | 4 | 4 | 3 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 1 | 0 | 1 |
| Not Hispanic or Latino | 3 | 5 | 2 |
| Unknown or Not Reported | 0 | 0 | 0 |

| Reporting group values | MEDI0680 2.5 mg/kg + Durvalumab 10 mg | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg |
|--|---------------------------------------|--------------------------------------|--------------------------------------|
| Number of subjects | 3 | 9 | 6 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 2 | 7 | 1 |
| From 65-84 years | 1 | 1 | 5 |
| 85 years and over | 0 | 1 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 62.3 | 62.1 | 69.5 |
| standard deviation | ± 11.6 | ± 11.0 | ± 9.9 |

| | | | |
|---|---|---|---|
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 1 | 5 | 2 |
| Male | 2 | 4 | 4 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 0 | 0 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 1 | 0 |
| Black or African American | 0 | 0 | 0 |
| White | 2 | 8 | 6 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 1 | 0 | 0 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 2 | 0 |
| Not Hispanic or Latino | 2 | 7 | 6 |
| Unknown or Not Reported | 1 | 0 | 0 |

| Reporting group values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg |
|--|-------------------|---------------------------------------|------------------|
| Number of subjects | 4 | 42 | 21 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 2 | 21 | 17 |
| From 65-84 years | 2 | 21 | 4 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 64.8 | 61.0 | 59.1 |
| standard deviation | ± 14.2 | ± 9.8 | ± 10.5 |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 1 | 9 | 6 |
| Male | 3 | 33 | 15 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 0 | 0 |
| Asian | 0 | 1 | 0 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 0 | 3 |
| White | 3 | 34 | 16 |
| More than one race | 0 | 0 | 0 |

| | | | |
|-------------------------|---|----|----|
| Unknown or Not Reported | 0 | 7 | 2 |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 1 | 1 |
| Not Hispanic or Latino | 4 | 40 | 20 |
| Unknown or Not Reported | 0 | 1 | 0 |

| | | | |
|---|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 97 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 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) | 56 | | |
| From 65-84 years | 40 | | |
| 85 years and over | 1 | | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 29 | | |
| Male | 68 | | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 1 | | |
| Asian | 2 | | |
| Native Hawaiian or Other Pacific Islander | 1 | | |
| Black or African American | 3 | | |
| White | 80 | | |
| More than one race | 0 | | |
| Unknown or Not Reported | 10 | | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 6 | | |
| Not Hispanic or Latino | 89 | | |
| Unknown or Not Reported | 2 | | |

End points

End points reporting groups

| | |
|---|---------------------------------------|
| Reporting group title | MEDI0680 0.1 mg/kg + Durvalumab 3 mg |
| Reporting group description: Participants in dose-escalation phase received IV infusion of MEDI0680 0.1 mg/kg and durvalumab 3 mg/kg every 2 weeks (Q2W) for up to 12 months. | |
| Reporting group title | MEDI0680 0.1 mg/kg + Durvalumab 10 mg |
| Reporting group description: Participants in dose-escalation phase received IV infusion of MEDI0680 0.1 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months. | |
| Reporting group title | MEDI0680 0.5 mg/kg + Durvalumab 10 mg |
| Reporting group description: Participants in dose-escalation phase received IV infusion of MEDI0680 0.5 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months. | |
| Reporting group title | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
| Reporting group description: Participants in dose-escalation phase received IV infusion of MEDI0680 2.5 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months. | |
| Reporting group title | MEDI0680 10 mg/kg + Durvalumab 10 mg |
| Reporting group description: Participants in dose-escalation phase received IV infusion of MEDI0680 10 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months. | |
| Reporting group title | MEDI0680 20 mg/kg + Durvalumab 10 mg |
| Reporting group description: Participants in dose-escalation phase received IV infusion of MEDI0680 20 mg/kg and durvalumab 10 mg/kg Q2W for up to 12 months. | |
| Reporting group title | MEDI0680 20 mg/kg |
| Reporting group description: Participants in dose-expansion phase received IV infusion of MEDI0680 20 mg/kg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first. | |
| Reporting group title | MEDI0680 20 mg/kg + Durvalumab 750 mg |
| Reporting group description: Participants in dose-expansion phase received IV infusion of MEDI0680 20 mg/kg and durvalumab 750 mg/kg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first. | |
| Reporting group title | Nivolumab 240 mg |
| Reporting group description: Participants in dose-expansion phase received IV infusion of nivolumab 240 mg Q2W until unacceptable toxicity, confirmed disease progression, development of other reason for treatment discontinuation, or for a maximum of 2 years, whichever occurred first. | |

Primary: Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs) in Dose-escalation Phase

| | |
|-----------------|---|
| End point title | Number of Participants With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs) in Dose-escalation Phase ^{[1][2]} |
|-----------------|---|

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. An SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. The TEAEs are defined as events present at baseline that

worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. As-treated population (participants who received any study drug [MEDI0680, durvalumab, or nivolumab] and grouped according to actual treatment received) was analysed for this end point.

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: | |
| Day 1 through 90 days post end of treatment (approximately 5 years 10 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for the end points.

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|-----------------------------|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: Participants | | | | |
| Any TEAE | 4 | 5 | 3 | 3 |
| Any TESA | 1 | 1 | 1 | 2 |

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg | | |
|-----------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: Participants | | | | |
| Any TEAE | 9 | 6 | | |
| Any TESA | 6 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Abnormal Clinical Laboratory Parameters Reported as TEAEs in Dose-escalation Phase

| | |
|-----------------|--|
| End point title | Number of Participants With Abnormal Clinical Laboratory Parameters Reported as TEAEs in Dose-escalation Phase ^{[3][4]} |
|-----------------|--|

End point description:

Number of participants in dose-escalation phase with abnormal clinical laboratory parameters reported as TEAEs are reported. Abnormal clinical laboratory parameters are defined as any abnormal finding during analysis of serum chemistry, hematology, coagulation, and urine. As-treated population (participants who received any study drug [MEDI0680, durvalumab, or nivolumab] and grouped according to actual treatment received) was analysed for this end point.

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

End point timeframe:

Day 1 through 90 days post end of treatment (approximately 5 years 10 months)

Notes:

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

Justification: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for the end points.

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|---|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: Participants | | | | |
| Anaemia | 0 | 0 | 1 | 1 |
| Iron deficiency anaemia | 0 | 0 | 0 | 0 |
| Leukocytosis | 1 | 0 | 0 | 0 |
| Lymphopenia | 0 | 0 | 0 | 0 |
| Activated partial thromboplastin time prolonged | 0 | 0 | 0 | 0 |
| Blood fibrinogen decreased | 1 | 0 | 0 | 0 |
| International normalized ratio | 0 | 0 | 0 | 0 |
| Lymphocyte count decreased | 0 | 0 | 0 | 0 |
| Prothrombin time prolonged | 0 | 0 | 0 | 0 |
| White blood cell count decreased | 0 | 0 | 0 | 0 |
| Alanine aminotransferase increased | 0 | 0 | 0 | 0 |
| Amylase increased | 0 | 0 | 0 | 0 |
| Aspartate aminotransferase increased | 0 | 0 | 0 | 0 |
| Blood alkaline phosphatase increased | 1 | 0 | 1 | 0 |
| Blood creatinine increased | 0 | 0 | 0 | 0 |
| Blood phosphorus decreased | 1 | 0 | 0 | 0 |
| Blood urea increased | 0 | 0 | 0 | 0 |
| Gamma glutamyltransferase increased | 0 | 0 | 0 | 0 |
| Lipase increased | 1 | 0 | 1 | 0 |
| Hypercalcaemia | 0 | 0 | 0 | 0 |
| Hyperglycaemia | 0 | 0 | 0 | 0 |
| Hyperkalaemia | 0 | 0 | 0 | 0 |
| Hypermagnesaemia | 0 | 0 | 1 | 0 |
| Hyperuricaemia | 1 | 0 | 0 | 0 |
| Hypoalbuminaemia | 0 | 0 | 0 | 0 |
| Hypokalaemia | 0 | 0 | 0 | 0 |
| Hypomagnesaemia | 0 | 0 | 0 | 0 |
| Hyponatraemia | 0 | 0 | 0 | 0 |
| proteinuria | 0 | 0 | 0 | 0 |

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 | MEDI0680 20 mg/kg + Durvalumab 10 | | |
|------------------|-----------------------------------|-----------------------------------|--|--|
|------------------|-----------------------------------|-----------------------------------|--|--|

| | mg | mg | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: Participants | | | | |
| Anaemia | 3 | 0 | | |
| Iron deficiency anaemia | 1 | 0 | | |
| Leukocytosis | 0 | 0 | | |
| Lymphopenia | 1 | 0 | | |
| Activated partial thromboplastin time prolonged | 0 | 1 | | |
| Blood fibrinogen decreased | 0 | 1 | | |
| International normalized ratio | 0 | 1 | | |
| Lymphocyte count decreased | 0 | 1 | | |
| Prothrombin time prolonged | 0 | 1 | | |
| White blood cell count decreased | 0 | 1 | | |
| Alanine aminotransferase increased | 1 | 0 | | |
| Amylase increased | 1 | 1 | | |
| Aspartate aminotransferase increased | 2 | 0 | | |
| Blood alkaline phosphatase increased | 1 | 0 | | |
| Blood creatinine increased | 2 | 1 | | |
| Blood phosphorus decreased | 0 | 0 | | |
| Blood urea increased | 1 | 0 | | |
| Gamma glutamyltransferase increased | 1 | 0 | | |
| Lipase increased | 1 | 0 | | |
| Hypercalcaemia | 1 | 1 | | |
| Hyperglycaemia | 1 | 0 | | |
| Hyperkalaemia | 1 | 0 | | |
| Hypermagnesaemia | 0 | 0 | | |
| Hyperuricaemia | 1 | 0 | | |
| Hypoalbuminaemia | 1 | 0 | | |
| Hypokalaemia | 2 | 0 | | |
| Hypomagnesaemia | 2 | 0 | | |
| Hyponatraemia | 2 | 1 | | |
| proteinuria | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Abnormal Vital Signs and Physical Examinations Reported as TEAES in Dose-escalation Phase

| | |
|-----------------|---|
| End point title | Number of Participants With Abnormal Vital Signs and Physical Examinations Reported as TEAES in Dose-escalation Phase ^{[5][6]} |
|-----------------|---|

End point description:

Number of participants in dose-escalation phase with abnormal vital signs reported as TEAEs are reported. Abnormal vital signs is defined as any abnormal finding in the vital sign parameters (blood pressure, heart rate, body temperature, and respiratory rate). Abnormal physical examination findings are defined as any abnormal finding in the following body systems: head and neck, respiratory, cardiovascular, gastrointestinal, urogenital, musculoskeletal, neurological, psychiatric, dermatological, hematologic/lymphatic, and endocrine systems, and weight. As-treated population (participants who received any study drug [MEDI0680, durvalumab, or nivolumab] and grouped according to actual treatment received) was analysed for this end point.

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

End point timeframe:

Day 1 through 90 days post end of treatment (approximately 5 years 10 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for the end points.

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|-----------------------------|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: Participants | | | | |
| Atrial fibrillation | 0 | 0 | 0 | 0 |
| Palpitations | 1 | 0 | 0 | 0 |
| Sinus tachycardia | 0 | 0 | 0 | 0 |
| Tachycardia | 0 | 0 | 0 | 0 |
| Pyrexia | 0 | 0 | 2 | 0 |
| Weight decreased | 0 | 0 | 0 | 0 |
| Hypertension | 1 | 0 | 0 | 0 |

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg | | |
|-----------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: Participants | | | | |
| Atrial fibrillation | 1 | 0 | | |
| Palpitations | 0 | 0 | | |
| Sinus tachycardia | 1 | 0 | | |
| Tachycardia | 0 | 1 | | |
| Pyrexia | 3 | 1 | | |
| Weight decreased | 1 | 1 | | |
| Hypertension | 1 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Abnormal Electrocardiograms (ECGs) Reported as TEAEs in Dose-escalation Phase

| | |
|-----------------|---|
| End point title | Number of Participants With Abnormal Electrocardiograms (ECGs) Reported as TEAEs in Dose-escalation Phase ^{[7][8]} |
|-----------------|---|

End point description:

Number of participants in dose-escalation phase with abnormal ECG parameters reported as TEAEs are reported. As-treated population (participants who received any study drug [MEDI0680, durvalumab, or nivolumab] and grouped according to actual treatment received) was analysed for this end point.

End point type Primary

End point timeframe:

Day 1 through 90 days post end of treatment (approximately 5 years 10 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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for the end points.

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|-----------------------------|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: Participants | | | | |
| Palpitations | 1 | 0 | 0 | 0 |
| Atrial fibrillation | 0 | 0 | 0 | 0 |
| Sinus tachycardia | 0 | 0 | 0 | 0 |
| Pericardial effusion | 0 | 0 | 0 | 0 |
| Tachycardia | 0 | 0 | 0 | 0 |

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg | | |
|-----------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: Participants | | | | |
| Palpitations | 0 | 0 | | |
| Atrial fibrillation | 1 | 0 | | |
| Sinus tachycardia | 1 | 0 | | |
| Pericardial effusion | 1 | 0 | | |
| Tachycardia | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate (ORR) Based on Investigator-assessed Response Using Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) in Dose-expansion Phase

End point title Objective Response Rate (ORR) Based on Investigator-

End point description:

The ORR is defined as best overall response of confirmed complete response (CR) or confirmed partial response (PR) based on RECIST v1.1. The CR is defined as disappearance of all target and non-target lesions and no new lesions. The PR is defined as $\geq 30\%$ decrease in the sum of diameters of target lesions (compared to baseline) and no new non-target lesion. A confirmed CR or PR is defined as 2 CRs or 2 PRs that were separated by at least 4 weeks with no evidence of progression in-between. As-treated population was analysed for this end point.

End point type Primary

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or end of treatment (approximately 5 years 10 months)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg | |
|-----------------------------------|-------------------|---------------------------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 42 | 21 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 0 (0 to 60.2) | 16.7 (7.0 to 31.4) | 23.8 (8.2 to 47.2) | |

Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|--------------------------------------|
| Comparison groups | MEDI0680 20 mg/kg v Nivolumab 240 mg |
| Number of subjects included in analysis | 25 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5494 |
| Method | Fisher exact |
| Parameter estimate | Rate difference |
| Point estimate | -23.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -72.8 |
| upper limit | 31.1 |

| Statistical analysis title | Statistical Analysis 2 |
|----------------------------|--|
| Comparison groups | MEDI0680 20 mg/kg + Durvalumab 750 mg v Nivolumab 240 mg |

| | |
|---|-----------------|
| Number of subjects included in analysis | 63 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.513 |
| Method | Fisher exact |
| Parameter estimate | Rate difference |
| Point estimate | -7.1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -33.6 |
| upper limit | 20 |

Secondary: Best Overall Response (BOR) Based on Investigator-assessed RECIST v1.1 in Dose-expansion Phase

| | |
|-----------------|--|
| End point title | Best Overall Response (BOR) Based on Investigator-assessed RECIST v1.1 in Dose-expansion Phase ^[10] |
|-----------------|--|

End point description:

The BOR includes CR, PR, stable disease (SD), progressive disease (PD), and non-evaluable (NE) based on RECIST v1.1. The CR is defined as disappearance of all target and non-target lesions and no new lesions. The PR is defined as $\geq 30\%$ decrease in the sum of diameters of target lesions (compared to baseline) and no new nontarget lesion. The PD is defined at least 20% decrease in the sum of diameters of target lesions (compared to baseline) and/or new lesion. The SD is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for disease progression. The NE is defined as either when no or only a subset of lesion measurements are made at an assessment. As-treated population was analysed for this end point.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or end of treatment (approximately 5 years 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg | |
|-----------------------------|-------------------|---------------------------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 42 | 21 | |
| Units: Participants | | | | |
| CR | 0 | 2 | 0 | |
| PR | 0 | 5 | 5 | |
| SD | 3 | 17 | 8 | |
| PD | 1 | 17 | 6 | |
| NE | 0 | 1 | 2 | |

Statistical analyses

Secondary: Disease Control Rate (DCR) Based on Investigator-assessed RECIST v1.1 in Dose-expansion Phase

| | |
|-----------------|---|
| End point title | Disease Control Rate (DCR) Based on Investigator-assessed RECIST v1.1 in Dose-expansion Phase ^[11] |
|-----------------|---|

End point description:

The DCR is defined as a BOR of confirmed CR, confirmed PR, or SD based on RECIST v1.1. A confirmed CR is defined as two CRs (disappearance of all target and non-target lesions and no new lesions) that were separated by at least 4 weeks with no evidence of progression in-between. A confirmed PR is defined as two PRs ($\geq 30\%$ decrease in the sum of diameters of target lesions compared to baseline and no new non-target lesion) that were separated by at least 4 weeks with no evidence of progression in-between. The SD is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for disease progression. The DCR at ≥ 8 weeks and ≥ 24 weeks are reported. As-treated population was analysed for this end point.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or end of treatment (approximately 5 years 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg | |
|-----------------------------------|---------------------|---------------------------------------|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 42 | 21 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| DCR at ≥ 8 weeks | 75.0 (19.4 to 99.4) | 57.1 (41.0 to 72.3) | 61.9 (38.4 to 81.9) | |
| DCR at ≥ 24 weeks | 50.0 (6.8 to 93.2) | 38.1 (23.6 to 54.4) | 38.1 (18.1 to 61.6) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR) Based on Investigator-assessed RECIST v1.1 in Dose-expansion Phase

| | |
|-----------------|---|
| End point title | Time to Response (TTR) Based on Investigator-assessed RECIST v1.1 in Dose-expansion Phase ^[12] |
|-----------------|---|

End point description:

The TTR is defined as the time from the first dose of treatment until the first documentation of a subsequently confirmed OR (confirmed CR or confirmed PR) based on RECIST v1.1. A confirmed CR is defined as two CRs (disappearance of all target and non-target lesions and no new lesions) that were separated by at least 4 weeks with no evidence of progression in-between. A confirmed PR is defined as two PRs ($\geq 30\%$ decrease in the sum of diameters of target lesions compared to baseline and no new non-target lesion) that were separated by at least 4 weeks with no evidence of progression in-between. The TTR was estimated using Kaplan-Meier method. The TTR was analysed for participants from As-treated population who achieved OR.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or end of treatment (approximately 5 years 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg | |
|----------------------------------|-------------------|---------------------------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[13] | 7 | 5 | |
| Units: Months | | | | |
| median (confidence interval 95%) | (to) | 1.8 (1.7 to 9.1) | 1.8 (1.6 to 7.3) | |

Notes:

[13] - No participant had achieved OR.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) Based on Investigator-assessed RECIST v1.1 in Dose-expansion Phase

| | |
|-----------------|---|
| End point title | Duration of Response (DoR) Based on Investigator-assessed RECIST v1.1 in Dose-expansion Phase ^[14] |
|-----------------|---|

End point description:

The DoR is defined as duration from the first documentation of OR (confirmed CR or confirmed PR) to the first documented disease progression based on RECIST v1.1 or death due to any cause, whichever occurred first. The confirmed CR or confirmed PR means 2 CRs (disappearance of all target and non-target lesions and no new lesions) or 2 PRs ($\geq 30\%$ decrease in the sum of diameters of target lesions compared to baseline and no new non-target lesion) that were separated by at least 4 weeks with no evidence of progression in-between; and PD means at least 20% decrease in the sum of diameters of target lesions (compared to baseline) and/or new lesion. The DoR was estimated using Kaplan-Meier method. The arbitrary numbers 99.999 and 99999 signified the data for median and upper limit of confidence interval could not be derived due to insufficient events being observed at the time of the analysis. The DoR was analysed for participants from As-treated population who achieved OR.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or end of treatment (approximately 5 years 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg | |
|----------------------------------|-------------------|---------------------------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[15] | 7 | 5 | |
| Units: Months | | | | |
| median (confidence interval 95%) | (to) | 99.999 (12.9 to 99999) | 99.999 (4.4 to 99999) | |

Notes:

[15] - No participant had achieved OR in this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) Based on Investigator-assessed RECIST v1.1 in Dose-expansion Phase

| | |
|-----------------|--|
| End point title | Progression Free Survival (PFS) Based on Investigator-assessed RECIST v1.1 in Dose-expansion Phase ^[16] |
|-----------------|--|

End point description:

The PFS is defined as the time from the start of study treatment until the first documentation of disease progression based on RECIST v1.1 or death due to any cause, whichever occurred first. The PFS was estimated using Kaplan-Meier method. As-treated population (participants who received any study drug [MEDI0680, durvalumab, or nivolumab] and grouped according to actual treatment received) was analysed for this end point.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or end of treatment (approximately 5 years 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg | |
|----------------------------------|-------------------|---------------------------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 42 | 21 | |
| Units: Months | | | | |
| median (confidence interval 95%) | 5.5 (2.2 to 7.4) | 3.6 (2.0 to 5.5) | 3.6 (1.9 to 13.0) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival in Dose-expansion Phase

| | |
|-----------------|--|
| End point title | Overall Survival in Dose-expansion Phase ^[17] |
|-----------------|--|

End point description:

The OS is defined as the time from the start of study treatment until death due to any cause. The OS was estimated using Kaplan-Meier method. The arbitrary numbers 99.999, 0.9999, and 99999 signified the data for median, and lower and upper limit of confidence interval could not be derived due to insufficient number of events being observed at the time of the analysis. As-treated population (participants who received any study drug [MEDI0680, durvalumab, or nivolumab] and grouped according to actual treatment received) was analysed for this end point.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or end of treatment (approximately 5 years 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg | |
|----------------------------------|--------------------|---------------------------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 42 | 21 | |
| Units: Months | | | | |
| median (confidence interval 95%) | 19.9 (7.0 to 19.9) | 99.999 (0.9999 to 99999) | 99.999 (12.0 to 99999) | |

Statistical analyses

No statistical analyses for this end point

Secondary: BOR Based on Investigator-assessed Modified RECIST v1.1 in Dose-escalation Phase

| | |
|-----------------|--|
| End point title | BOR Based on Investigator-assessed Modified RECIST v1.1 in Dose-escalation Phase ^[18] |
|-----------------|--|

End point description:

The BOR includes CR, PR, SD, PD, and NE per Modified RECIST v1.1. The CR is defined as disappearance of all target and non-target lesions and no new lesions. The PR is defined as $\geq 30\%$ decrease in the sum of diameters of target lesions (compared to baseline) and no new nontarget lesion. The PD is defined at least 20% decrease in the sum of diameters of target lesions (compared to baseline) and/or new lesion. The SD is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for disease progression. The NE is defined as either when no or only a subset of lesion measurements are made at an assessment. As-treated population was analysed for this end point.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or EOT (approximately 12 months for each participant)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|-----------------------------|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: Participants | | | | |
| CR | 0 | 0 | 0 | 0 |
| PR | 2 | 0 | 1 | 0 |
| SD | 1 | 1 | 0 | 1 |
| PD | 1 | 3 | 2 | 1 |
| NE | 0 | 1 | 0 | 1 |

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg | | |
|-----------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: Participants | | | | |
| CR | 1 | 0 | | |
| PR | 3 | 4 | | |
| SD | 2 | 1 | | |
| PD | 2 | 1 | | |
| NE | 1 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ORR Based on Investigator-assessed Modified RECIST v1.1 in Dose-escalation Phase

| | |
|-----------------|--|
| End point title | ORR Based on Investigator-assessed Modified RECIST v1.1 in Dose-escalation Phase ^[19] |
|-----------------|--|

End point description:

The ORR is defined as best overall response of confirmed CR or confirmed PR based on modified RECIST v1.1. The CR is defined as disappearance of all target and non-target lesions and no new lesions. The PR is defined as $\geq 30\%$ decrease in the sum of diameters of target lesions (compared to baseline) and no new non-target lesion. A confirmed CR or PR is defined as 2 CRs or 2 PRs that were separated by at least 4 weeks with no evidence of progression in-between. As-treated population was analysed for this end point.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or EOT (approximately 12 months for each participant)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|-----------------------------------|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 50.0 (6.8 to 93.2) | 0 (0 to 52.2) | 33.3 (0.8 to 90.6) | 0 (0 to 70.8) |

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg | | |
|-----------------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 44.4 (13.7 to 78.8) | 66.7 (22.3 to 95.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DCR Based on Investigator-assessed Modified RECIST v1.1 in Dose-escalation Phase

| | |
|-----------------|--|
| End point title | DCR Based on Investigator-assessed Modified RECIST v1.1 in Dose-escalation Phase ^[20] |
|-----------------|--|

End point description:

The DCR is defined as a BOR of confirmed CR, confirmed PR, or SD based on modified RECIST v1.1. A confirmed CR is defined as two CRs (disappearance of all target and non-target lesions and no new lesions) that were separated by at least 4 weeks with no evidence of progression in-between. A confirmed PR is defined as two PRs ($\geq 30\%$ decrease in the sum of diameters of target lesions compared to baseline and no new non-target lesion) that were separated by at least 4 weeks with no evidence of progression in-between. The SD is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for disease progression. The DCR at ≥ 8 weeks and ≥ 24 weeks are reported. As-treated population was analysed for this end point.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or EOT (approximately 12 months for each participant)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|-----------------------------------|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| DCR at ≥ 8 weeks | 75.0 (19.4 to 99.4) | 20.0 (0.5 to 71.6) | 33.3 (0.8 to 90.6) | 33.3 (0.8 to 90.6) |
| DCR at ≥ 24 weeks | 50.0 (6.8 to 93.2) | 0 (0 to 52.2) | 33.3 (0.8 to 90.6) | 0 (0 to 70.8) |

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg | | |
|-----------------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| DCR at ≥ 8 weeks | 66.7 (29.9 to 92.5) | 83.3 (35.9 to 99.6) | | |
| DCR at ≥ 24 weeks | 44.4 (13.7 to 78.8) | 83.3 (35.9 to 99.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: TTR Based on Investigator-assessed Modified RECIST v1.1 in Dose-escalation Phase

| | |
|-----------------|--|
| End point title | TTR Based on Investigator-assessed Modified RECIST v1.1 in Dose-escalation Phase ^[21] |
|-----------------|--|

End point description:

The TTR is defined as time from the first dose of treatment until the first documentation of a subsequently confirmed OR (confirmed CR or confirmed PR) based on modified RECIST v1.1. Confirmed CR or confirmed PR are defined as 2 CRs (disappearance of all target and non-target lesions and no new lesions) or 2 PRs ($\geq 30\%$ decrease in the sum of diameters of target lesions compared to baseline and no new non-target lesion) that were separated by at least 4 weeks with no evidence of progression in-between. The TTR was estimated using Kaplan-Meier method. As-treated population was analysed for this end point. The arbitrary numbers 0.9999 and 99999 signified the data for lower and upper limit of confidence interval could not be derived due to insufficient number of events being observed at the time of the analysis. The TTR was analysed for participants from As-treated population who achieved OR.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or EOT (approximately 12 months for each participant)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|----------------------------------|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2 | 0 ^[22] | 1 | 0 ^[23] |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.6 (1.6 to 3.5) | (to) | 3.4 (0.9999 to 99999) | (to) |

Notes:

[22] - No participant had achieved OR.

[23] - No participant had achieved OR.

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg | | |
|----------------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 4 | 4 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 3.5 (1.6 to 3.5) | 3.2 (1.7 to 10.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DoR Based on Investigator-assessed Modified RECIST v1.1 in Dose-escalation Phase

| | |
|-----------------|--|
| End point title | DoR Based on Investigator-assessed Modified RECIST v1.1 in Dose-escalation Phase ^[24] |
|-----------------|--|

End point description:

The DoR is defined as duration from the first documentation of OR (confirmed CR or confirmed PR) to the first documented disease progression based on RECIST v1.1 or death due to any cause, whichever occurred first. Confirmed CR or confirmed PR are defined as 2 CRs (disappearance of all target and non-target lesions and no new lesions) or 2 PRs ($\geq 30\%$ decrease in the sum of diameters of target lesions compared to baseline and no new non-target lesion) that were separated by at least 4 weeks with no evidence of progression in-between. The DoR was estimated using Kaplan-Meier method. The arbitrary numbers 99.999, 0.9999, and 99999 signified data for median, and lower and upper limit of confidence interval could not be derived due to insufficient number of events being observed at the time of the analysis. The DoR was analysed for participants from As-treated population who achieved OR.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or EOT (approximately 12 months for each participant)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|----------------------------------|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 2 | 0 ^[25] | 1 | 0 ^[26] |
| Units: Months | | | | |
| median (confidence interval 95%) | 16.8 (0.9999 to 99999) | (to) | 99.999 (0.9999 to 99999) | (to) |

Notes:

[25] - No participant had achieved OR.

[26] - No participant had achieved OR.

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg | | |
|----------------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 4 | 4 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 7.4 (5.6 to 99999) | 99.999 (5.6 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS Based on Investigator-assessed Modified RECIST v1.1 in Dose-escalation Phase

| | |
|-----------------|--|
| End point title | PFS Based on Investigator-assessed Modified RECIST v1.1 in Dose-escalation Phase ^[27] |
|-----------------|--|

End point description:

The PFS is defined as the time from the start of study treatment until the first documentation of disease progression based on modified RECIST v1.1 or death due to any cause, whichever occurred first. The arbitrary number 99999 signified the data for upper limit of confidence interval could not be derived due to insufficient number of events being observed at the time of the analysis. The PFS was estimated using Kaplan-Meier method. As-treated population was analysed for this end point.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or EOT (approximately 12 months for each participant)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|----------------------------------|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: Months | | | | |
| median (confidence interval 95%) | 20.2 (1.6 to 20.2) | 1.7 (1.6 to 3.5) | 1.6 (1.6 to 99999) | 1.8 (1.5 to 3.4) |

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg | | |
|----------------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 7.0 (1.6 to 99999) | 23.4 (1.8 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: OS in Dose-escalation Phase

| | |
|-----------------|---|
| End point title | OS in Dose-escalation Phase ^[28] |
|-----------------|---|

End point description:

The OS is defined as the time from the start of study treatment until death due to any cause. The OS was estimated using Kaplan-Meier method. The arbitrary numbers 99.999, 0.9999, and 99999 signified the data for median, and lower and upper limit of confidence interval could not be derived due to insufficient number of events being observed at the time of the analysis. As-treated population was analysed for this end point.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or EOT (approximately 12 months for each participant)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|----------------------------------|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: Months | | | | |
| median (confidence interval 95%) | 16.3 (3.6 to 99999) | 99.999 (4.2 to 99999) | 14.7 (0.9999 to 99999) | 7.9 (1.5 to 7.9) |

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg | | |
|----------------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 6 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 12.8 (3.1 to 99999) | 99.999 (29.6 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With TEAEs and TSEAEs in Dose-expansion Phase

| | |
|-----------------|--|
| End point title | Number of Participants With TEAEs and TSEAEs in Dose-expansion Phase ^[29] |
|-----------------|--|

End point description:

An AE is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. An SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. The TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. As-treated population (participants who received any study drug [MEDI0680, durvalumab, or nivolumab] and grouped according to actual treatment received) was analysed for this end point.

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

End point timeframe:

Day 1 through 90 days post end of treatment (approximately 5 years 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg | |
|-----------------------------|-------------------|---------------------------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 42 | 21 | |
| Units: Participants | | | | |
| Any TEAE | 4 | 42 | 20 | |
| Any TSEAE | 3 | 22 | 13 | |

Statistical analyses

Secondary: Number of Participants With Abnormal Clinical Laboratory Parameters Reported as TEAEs in Dose-expansion Phase

| | |
|-----------------|---|
| End point title | Number of Participants With Abnormal Clinical Laboratory Parameters Reported as TEAEs in Dose-expansion Phase ^[30] |
|-----------------|---|

End point description:

Number of participants in dose-expansion phase with abnormal clinical laboratory parameters reported as TEAEs are reported. Abnormal clinical laboratory parameters defined as any abnormal finding during analysis of serum chemistry, hematology, coagulation, and urine. As-treated population (participants who received any study drug [MEDI0680, durvalumab, or nivolumab] and grouped according to actual treatment received) was analysed for this end point.

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

End point timeframe:

Day 1 through 90 days post end of treatment (approximately 5 years 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg | |
|--|-------------------|---------------------------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 42 | 21 | |
| Units: Participants | | | | |
| Anaemia | 1 | 6 | 5 | |
| Neutropenia | 0 | 1 | 0 | |
| Blood iron decreased | 0 | 0 | 1 | |
| Lymphocyte count decreased | 0 | 0 | 1 | |
| Neutrophil count decreased | 1 | 1 | 0 | |
| Platelet count decreased | 0 | 0 | 1 | |
| Platelet count increased | 0 | 0 | 1 | |
| Prothrombin time prolonged | 0 | 0 | 1 | |
| White blood cell count increased | 0 | 0 | 1 | |
| Alanine aminotransferase increased | 1 | 1 | 3 | |
| Amylase decreased | 0 | 0 | 1 | |
| Amylase increased | 1 | 3 | 3 | |
| Aspartate aminotransferase increased | 1 | 2 | 3 | |
| Blood alkaline phosphatase increased | 0 | 0 | 1 | |
| Blood bilirubin increased | 0 | 0 | 1 | |
| Blood creatine increased | 1 | 1 | 0 | |
| Blood creatine phosphokinase increased | 0 | 1 | 0 | |
| Blood creatinine increased | 1 | 4 | 3 | |
| Blood glucose increased | 0 | 0 | 1 | |
| Blood triglycerides increased | 0 | 1 | 1 | |
| C-reactive protein increased | 0 | 1 | 1 | |
| Lipase increased | 1 | 4 | 2 | |
| Transaminases increased | 0 | 1 | 0 | |
| Hypercalcaemia | 0 | 6 | 2 | |
| Hyperglycaemia | 0 | 1 | 0 | |
| Hyperkalaemia | 0 | 2 | 2 | |

| | | | | |
|---|---|---|---|--|
| Hypertriglyceridaemia | 0 | 1 | 0 | |
| Hypoalbuminaemia | 0 | 2 | 0 | |
| Hypocalcaemia | 0 | 1 | 0 | |
| Hypoglycaemia | 0 | 1 | 0 | |
| Hypokalaemia | 0 | 5 | 2 | |
| Hypomagnesaemia | 0 | 4 | 2 | |
| Hyponatraemia | 1 | 3 | 1 | |
| Hypophosphataemia | 0 | 1 | 3 | |
| Urine abnormality | 0 | 1 | 0 | |
| Blood thyroid stimulating hormone increased | 0 | 2 | 2 | |
| Blood urine present | 0 | 0 | 1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Vital Signs and Physical Examinations Reported as TEAEs in Dose-expansion Phase

| | |
|-----------------|--|
| End point title | Number of Participants With Abnormal Vital Signs and Physical Examinations Reported as TEAEs in Dose-expansion Phase ^[31] |
|-----------------|--|

End point description:

Number of participants in dose-expansion phase with abnormal vital signs reported as TEAEs are reported. Abnormal vital signs is defined as any abnormal finding in the vital sign parameters (blood pressure, heart rate, body temperature, and respiratory rate). Abnormal physical examination findings are defined as any abnormal finding in the following body systems: head and neck, respiratory, cardiovascular, gastrointestinal, urogenital, musculoskeletal, neurological, psychiatric, dermatological, hematologic/lymphatic, and endocrine systems, and weight. As-treated population (participants who received any study drug [MEDI0680, durvalumab, or nivolumab] and grouped according to actual treatment received) was analysed for this end point.

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

End point timeframe:

Day 1 through 90 days post end of treatment (approximately 5 years 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg | |
|-----------------------------|-------------------|---------------------------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 42 | 21 | |
| Units: Participants | | | | |
| Atrial fibrillation | 0 | 2 | 1 | |
| Tachycardia | 0 | 1 | 0 | |
| Pyrexia | 2 | 9 | 2 | |
| Weight decreased | 0 | 5 | 0 | |
| Weight increased | 0 | 3 | 0 | |
| Hypoxia | 0 | 1 | 1 | |
| Hypertension | 1 | 5 | 0 | |

| | | | | |
|-------------|---|---|---|--|
| Hypotension | 1 | 2 | 1 | |
|-------------|---|---|---|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal ECGs Reported as TEAEs in Dose-expansion Phase

| | |
|-----------------|---|
| End point title | Number of Participants With Abnormal ECGs Reported as TEAEs in Dose-expansion Phase ^[32] |
|-----------------|---|

End point description:

Number of participants in dose-expansion phase with abnormal ECG parameters reported as TEAEs are reported. As-treated population (participants who received any study drug [MEDI0680, durvalumab, or nivolumab] and grouped according to actual treatment received) was analysed for this end point.

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

End point timeframe:

Day 1 through 90 days post end of treatment (approximately 5 years 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg | |
|-----------------------------|-------------------|---------------------------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 42 | 21 | |
| Units: Participants | | | | |
| Angina pectoris | 1 | 1 | 0 | |
| Tachycardia | 0 | 1 | 0 | |
| Atrial fibrillation | 0 | 2 | 1 | |
| Cardiac failure congestive | 0 | 0 | 1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of MEDI0680 in Dose-escalation and Dose-expansion Phases

| | |
|-----------------|--|
| End point title | Serum Concentration of MEDI0680 in Dose-escalation and Dose-expansion Phases ^[33] |
|-----------------|--|

End point description:

Serum concentration of MEDI0680 were assessed using parameters Cmin (pre-dose) and Cmax (end of infusion), where Cmin was trough concentration and Cmax was peak concentration. Participants from As-treated population who received MEDI0680, grouped according to actual treatment received, and had quantifiable and calculable serum samples at the specified time points were analysed for this end point.

The arbitrary number 9999.9 signified the sample was not quantifiable and therefore, not calculable. The arbitrary number 0.0009 signified no data as no participants were analysed for the specified time points. Here, 'n' denotes the number of participants analysed at the specified time points.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Pre-dose and end of infusion on Cycle 1 Day 1, Cycle 1 Day 15, and Cycle 2 Day 1 | |

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|---|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cmin at Cycle1 Day1 (n = 4, 5, 3, 3, 9, 6, 4, 40) | 9999.9 (± 9999.9) | 9999.9 (± 9999.9) | 9999.9 (± 9999.9) | 9999.9 (± 9999.9) |
| Cmax at Cycle1 Day1 (n = 4, 5, 3, 3, 9, 4, 4, 38) | 4.330 (± 26.18) | 3.877 (± 54.68) | 16.36 (± 26.46) | 69.28 (± 24.76) |
| Cmin at Cycle1 Day15 (n = 4, 3, 3, 3, 8, 5, 0, 0) | 1.143 (± 22.70) | 0.9937 (± 35.93) | 4.428 (± 62.38) | 18.67 (± 12.88) |
| Cmax at Cycle1 Day15 (n = 4, 3, 3, 3, 8, 5, 0, 0) | 5.420 (± 21.61) | 3.835 (± 25.30) | 20.52 (± 26.26) | 87.78 (± 20.69) |
| Cmin at Cycle2 Day1 (n = 4, 4, 3, 3, 7, 6, 4, 36) | 1.645 (± 49.08) | 1.361 (± 38.07) | 7.879 (± 52.74) | 31.81 (± 4.480) |
| Cmax at Cycle2 Day1 (n = 4, 4, 3, 3, 7, 6, 4, 34) | 3.515 (± 145.9) | 3.688 (± 80.17) | 17.28 (± 56.32) | 92.07 (± 17.72) |

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg |
|---|--------------------------------------|--------------------------------------|-------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 6 | 4 | 40 |
| Units: µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cmin at Cycle1 Day1 (n = 4, 5, 3, 3, 9, 6, 4, 40) | 9999.9 (± 9999.9) | 9999.9 (± 9999.9) | 9999.9 (± 9999.9) | 9999.9 (± 9999.9) |
| Cmax at Cycle1 Day1 (n = 4, 5, 3, 3, 9, 4, 4, 38) | 272.4 (± 24.62) | 529.9 (± 29.84) | 668.8 (± 21.04) | 135.9 (± 4007) |
| Cmin at Cycle1 Day15 (n = 4, 3, 3, 3, 8, 5, 0, 0) | 46.87 (± 559.4) | 205.8 (± 24.56) | 0.0009 (± 0.0009) | 0.0009 (± 0.0009) |
| Cmax at Cycle1 Day15 (n = 4, 3, 3, 3, 8, 5, 0, 0) | 348.1 (± 27.78) | 716.8 (± 26.72) | 0.0009 (± 0.0009) | 0.0009 (± 0.0009) |
| Cmin at Cycle2 Day1 (n = 4, 4, 3, 3, 7, 6, 4, 36) | 155.7 (± 24.20) | 378.0 (± 17.95) | 308.6 (± 30.45) | 253.9 (± 52.11) |
| Cmax at Cycle2 Day1 (n = 4, 4, 3, 3, 7, 6, 4, 34) | 440.7 (± 28.18) | 860.8 (± 13.82) | 936.1 (± 24.91) | 586.6 (± 63.42) |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Durvalumab in Dose-escalation and Dose-expansion Phases

| | |
|-----------------|--|
| End point title | Serum Concentration of Durvalumab in Dose-escalation and Dose-expansion Phases ^[34] |
|-----------------|--|

End point description:

Serum concentration of durvalumab were assessed using parameters Cmin (pre-dose) and Cmax (end of infusion), where Cmin was trough concentration and Cmax was peak concentration. Participants from As-treated population who received durvalumab, grouped according to actual treatment received, and had quantifiable and calculable serum samples at the specified time points were analysed for this end point. The arbitrary number 9999.9 signified the sample was not quantifiable and therefore, not calculable. The arbitrary number 0.0009 signified no data as no participants were analysed for the specified time points. Here, 'n' denotes the number of participants analysed at the specified time points.

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

End point timeframe:

Pre-dose and end of infusion on Cycle 1 Day 1, Cycle 1 Day 15, and Cycle 2 Day 1

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDIO680 0.1 mg/kg + Durvalumab 3 mg | MEDIO680 0.1 mg/kg + Durvalumab 10 mg | MEDIO680 0.5 mg/kg + Durvalumab 10 mg | MEDIO680 2.5 mg/kg + Durvalumab 10 mg |
|---|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cmin at Cycle1 Day1 (n = 4, 5, 3, 3, 9, 6, 38) | 9999.9 (± 9999.9) | 9999.9 (± 9999.9) | 9999.9 (± 9999.9) | 9999.9 (± 9999.9) |
| Cmax at Cycle1 Day1 (n = 4, 5, 3, 3, 9, 6, 41) | 65.47 (± 10.02) | 216.1 (± 25.14) | 213.8 (± 9.943) | 188.0 (± 17.82) |
| Cmin at Cycle1 Day15 (n = 4, 3, 3, 3, 8, 6, 0) | 19.62 (± 16.49) | 63.02 (± 7.836) | 49.04 (± 80.97) | 86.10 (± 69.76) |
| Cmax at Cycle1 Day15 (n = 4, 3, 3, 3, 8, 6, 0) | 95.14 (± 12.79) | 245.8 (± 13.45) | 241.1 (± 30.90) | 225.0 (± 9.213) |
| Cmin at Cycle2 Day1 (n = 4, 4, 3, 3, 7, 6, 27) | 23.83 (± 14.35) | 83.76 (± 34.29) | 89.20 (± 56.00) | 136.3 (± 45.72) |
| Cmax at Cycle2 Day1 (n = 4, 4, 3, 3, 7, 6, 32) | 84.43 (± 17.13) | 280.9 (± 12.48) | 297.5 (± 42.41) | 267.0 (± 25.97) |

| | | | | |
|------------------|-------------|-------------|-------------|--|
| End point values | MEDIO680 10 | MEDIO680 20 | MEDIO680 20 | |
|------------------|-------------|-------------|-------------|--|

| | mg/kg + Durvalumab 10 mg | mg/kg + Durvalumab 10 mg | mg/kg + Durvalumab 750 mg | |
|--|--------------------------------|--------------------------------|---------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 9 | 6 | 41 | |
| Units: µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cmin at Cycle1 Day1 (n = 4, 5, 3, 3, 9, 6, 38) | 9999.9 (± 9999.9) | 9999.9 (± 9999.9) | 9999.9 (± 9999.9) | |
| Cmax at Cycle1 Day1 (n = 4, 5, 3, 3, 9, 6, 41) | 248.0 (± 27.20) | 253.9 (± 11.35) | 186.9 (± 33.42) | |
| Cmin at Cycle1 Day15 (n = 4, 3, 3, 3, 8, 6, 0) | 79.59 (± 63.46) | 70.31 (± 22.00) | 0.0009 (± 0.0009) | |
| Cmax at Cycle1 Day15 (n = 4, 3, 3, 3, 8, 6, 0) | 292.7 (± 33.84) | 321.8 (± 23.05) | 0.0009 (± 0.0009) | |
| Cmin at Cycle2 Day1 (n = 4, 4, 3, 3, 7, 6, 27) | 124.8 (± 55.78) | 142.5 (± 50.52) | 78.41 (± 55.62) | |
| Cmax at Cycle2 Day1 (n = 4, 4, 3, 3, 7, 6, 32) | 370.9 (± 42.57) | 342.3 (± 18.08) | 258.1 (± 28.36) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-drug Antibodies (ADA) to MEDI0680 in Dose-escalation and Dose-expansion Phases

| | |
|-----------------|--|
| End point title | Number of Participants With Positive Anti-drug Antibodies (ADA) to MEDI0680 in Dose-escalation and Dose-expansion Phases ^[35] |
|-----------------|--|

End point description:

Number of participants with positive ADAs to MEDI0680 are reported. Persistent positive is defined as positive at ≥ 2 post-baseline assessments (with ≥ 16 weeks between first and last positive) or positive at last post-baseline assessment. Transient positive is defined as negative at last post-baseline assessment and positive at only one post-baseline assessment or at ≥ 2 post-baseline assessments (with < 16 weeks between first and last positive). As-treated population (participants who received MEDI0680 and grouped according to actual treatment received) was analysed for this end point.

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

End point timeframe:

Cycle 1 Day 1, Cycle 2 Day 1, Cycle 5 Day 1, Cycle 8 Day 1, Cycle 11 Day 1, 90 and 180 days post end of treatment (approximately 5 years and 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 0.1 mg/kg + Durvalumab 3 mg | MEDI0680 0.1 mg/kg + Durvalumab 10 mg | MEDI0680 0.5 mg/kg + Durvalumab 10 mg | MEDI0680 2.5 mg/kg + Durvalumab 10 mg |
|-----------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: Participants | | | | |
| ADA positive post-baseline | 2 | 0 | 2 | 0 |
| Persistent Positive | 2 | 0 | 2 | 0 |

| | | | | |
|--------------------|---|---|---|---|
| Transient Positive | 0 | 0 | 0 | 0 |
|--------------------|---|---|---|---|

| End point values | MEDIO680 10 mg/kg + Durvalumab 10 mg | MEDIO680 20 mg/kg + Durvalumab 10 mg | MEDIO680 20 mg/kg | MEDIO680 20 mg/kg + Durvalumab 750 mg |
|-----------------------------|--------------------------------------|--------------------------------------|-------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 8 | 6 | 4 | 39 |
| Units: Participants | | | | |
| ADA positive post-baseline | 0 | 0 | 0 | 2 |
| Persistent Positive | 0 | 0 | 0 | 0 |
| Transient Positive | 0 | 0 | 0 | 2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive ADA to Durvalumab in Dose-escalation and Dose-expansion Phases

| | |
|-----------------|---|
| End point title | Number of Participants With Positive ADA to Durvalumab in Dose-escalation and Dose-expansion Phases ^[36] |
|-----------------|---|

End point description:

Number of participants with positive ADA to durvalumab are reported. Persistent positive is defined as positive at ≥ 2 post-baseline assessments (with ≥ 16 weeks between first and last positive) or positive at last post-baseline assessment. Transient positive is defined as negative at last post-baseline assessment and positive at only one post-baseline assessment or at ≥ 2 post-baseline assessments (with < 16 weeks between first and last positive). As-treated population (participants who received durvalumab and grouped according to actual treatment received) was analysed for this end point.

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

End point timeframe:

Cycle 1 Day 1, Cycle 2 Day 1, Cycle 5 Day 1, Cycle 8 Day 1, Cycle 11 Day 1, 90 and 180 days post end of treatment (approximately 5 years and 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDIO680 0.1 mg/kg + Durvalumab 3 mg | MEDIO680 0.1 mg/kg + Durvalumab 10 mg | MEDIO680 0.5 mg/kg + Durvalumab 10 mg | MEDIO680 2.5 mg/kg + Durvalumab 10 mg |
|-----------------------------|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 5 | 3 | 3 |
| Units: Participants | | | | |
| ADA positive post-baseline | 1 | 0 | 0 | 0 |
| Persistent Positive | 1 | 0 | 0 | 0 |
| Transient Positive | 0 | 0 | 0 | 0 |

| End point values | MEDI0680 10 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 10 mg | MEDI0680 20 mg/kg + Durvalumab 750 mg | |
|-----------------------------|--------------------------------------|--------------------------------------|---------------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 8 | 6 | 39 | |
| Units: Participants | | | | |
| ADA positive post-baseline | 0 | 0 | 2 | |
| Persistent Positive | 0 | 0 | 2 | |
| Transient Positive | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: ORR for Participants With Programmed Cell Death Ligand 1 (PD-L1) Status Positive and Negative in Dose-expansion Phase

| | |
|-----------------|---|
| End point title | ORR for Participants With Programmed Cell Death Ligand 1 (PD-L1) Status Positive and Negative in Dose-expansion Phase ^[37] |
|-----------------|---|

End point description:

ORR for participants with PD-L1 status positive and negative are reported. The ORR is defined as best overall response of confirmed CR or confirmed PR based on RECIST v1.1. The CR is defined as disappearance of all target and non-target lesions and no new lesions. The PR is defined as $\geq 30\%$ decrease in the sum of diameters of target lesions (compared to baseline) and no new non-target lesion. A confirmed CR or PR is defined as 2 CRs or 2 PRs that were separated by at least 4 weeks with no evidence of progression in-between. Participants from As-treated population with PD-L1 positive ($> 1\%$ tumor cell membrane or $> 1\%$ immune cell staining) and PD-L1 negative ($\leq 1\%$ tumor cell membrane and $\leq 1\%$ immune cell staining) were analysed for this end point.

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

End point timeframe:

From baseline (Day -42 to Day -1) through disease progression or end of treatment (approximately 5 years 10 months)

Notes:

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

Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

| End point values | MEDI0680 20 mg/kg | MEDI0680 20 mg/kg + Durvalumab 750 mg | Nivolumab 240 mg | |
|-----------------------------------|-------------------|---------------------------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 4 | 42 | 21 | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | | | | |
| Participants with PD-L1 positive | 0 (0 to 97.5) | 40.0 (5.3 to 85.3) | 37.5 (8.5 to 75.5) | |
| Participants with PD-L1 negative | 0 (0 to 70.8) | 13.5 (4.5 to 28.8) | 15.4 (1.9 to 45.4) | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 through 90 days post end of treatment (approximately 5 years 10 months)

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | MEDI0680 0.1 mg/kg Q2W + Durva 3 mg/kg Q2W |
|-----------------------|--|

Reporting group description: -

| | |
|-----------------------|---|
| Reporting group title | MEDI0680 0.1 mg/kg Q2W + Durva 10 mg/kg Q2W |
|-----------------------|---|

Reporting group description: -

| | |
|-----------------------|---|
| Reporting group title | MEDI0680 0.5 mg/kg Q2W + Durva 10 mg/kg Q2W |
|-----------------------|---|

Reporting group description: -

| | |
|-----------------------|---|
| Reporting group title | MEDI0680 2.5 mg/kg Q2W + Durva 10 mg/kg Q2W |
|-----------------------|---|

Reporting group description: -

| | |
|-----------------------|--|
| Reporting group title | MEDI0680 10 mg/kg Q2W + Durva 10 mg/kg Q2W |
|-----------------------|--|

Reporting group description: -

| | |
|-----------------------|--|
| Reporting group title | MEDI0680 20 mg/kg Q2W + Durva 10 mg/kg Q2W |
|-----------------------|--|

Reporting group description: -

| | |
|-----------------------|-----------------------|
| Reporting group title | MEDI0680 20 mg/kg Q2W |
|-----------------------|-----------------------|

Reporting group description: -

| | |
|-----------------------|--|
| Reporting group title | MEDI0680 20 mg/kg Q2W + Durva 750 mg Q2W |
|-----------------------|--|

Reporting group description: -

| | |
|-----------------------|---------------------|
| Reporting group title | Nivolumab 240mg Q2W |
|-----------------------|---------------------|

Reporting group description: -

| Serious adverse events | MEDI0680 0.1 mg/kg Q2W + Durva 3 mg/kg Q2W | MEDI0680 0.1 mg/kg Q2W + Durva 10 mg/kg Q2W | MEDI0680 0.5 mg/kg Q2W + Durva 10 mg/kg Q2W |
|---|--|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | 1 / 3 (33.33%) |
| number of deaths (all causes) | 2 | 2 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastases to bone | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (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 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |

| | | | |
|---|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 | | | |
| Aphasia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrospinal fluid leakage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis autoimmune | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intracranial mass | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |

| | | | |
|---|----------------|---------------|---------------|
| Eye pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (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 |
| Colitis microscopic | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 enterocolitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 pancreatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 | | | |
| Diabetic foot | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia of malignancy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---------------|---------------|---------------|
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| 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 | MEDI0680 2.5 mg/kg Q2W + Durva 10 mg/kg Q2W | MEDI0680 10 mg/kg Q2W + Durva 10 mg/kg Q2W | MEDI0680 20 mg/kg Q2W + Durva 10 mg/kg Q2W |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 6 / 9 (66.67%) | 0 / 6 (0.00%) |
| number of deaths (all causes) | 2 | 5 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastases to bone | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to central nervous system | | | |

| | | | |
|--|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---------------|----------------|---------------|
| Pyrexia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |

| | | | |
|---|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Hip fracture | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (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 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|---------------|
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrospinal fluid leakage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis autoimmune | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intracranial mass | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |

| | | | |
|---|----------------|----------------|---------------|
| Eye pain | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis microscopic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune-mediated pancreatitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |

| | | | |
|---|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Diabetic foot | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |

| | | | |
|---|---------------|----------------|---------------|
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia of malignancy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (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 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---------------|---------------|---------------|
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |

| | | | |
|---|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | MEDI0680 20 mg/kg Q2W | MEDI0680 20 mg/kg Q2W + Durva 750 mg Q2W | Nivolumab 240mg Q2W |
|--|-----------------------|--|---------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | 22 / 42 (52.38%) | 13 / 21 (61.90%) |
| number of deaths (all causes) | 2 | 9 | 4 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastases to bone | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Metastases to central nervous system | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (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 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Chills | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---------------|----------------|----------------|
| Pyrexia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Psychiatric disorders | | | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Injury, poisoning and procedural complications | | | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (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 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 | | | |
| Aphasia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrospinal fluid leakage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Encephalitis autoimmune | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Headache | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Intracranial mass | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Seizure | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (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 |
| Eye disorders | | | |

| | | | |
|---|----------------|----------------|----------------|
| Eye pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 2 / 21 (9.52%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis microscopic | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Immune-mediated pancreatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Small intestinal obstruction | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (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 |
| Hepatic haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Skin and subcutaneous tissue disorders | | | |
| Diabetic foot | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (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 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Endocrine disorders | | | |

| | | | |
|---|---------------|----------------|-----------------|
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Hypercalcaemia of malignancy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Back pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (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 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 3 / 21 (14.29%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |

| | | | |
|---|----------------|----------------|----------------|
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Pathological fracture | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Osteomyelitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Spinal cord infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Urinary tract infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 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 |
| Failure to thrive | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (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 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (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 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (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 |

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

| Non-serious adverse events | MEDI0680 0.1 mg/kg Q2W + Durva 3 mg/kg Q2W | MEDI0680 0.1 mg/kg Q2W + Durva 10 mg/kg Q2W | MEDI0680 0.5 mg/kg Q2W + Durva 10 mg/kg Q2W |
|---|--|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | 5 / 5 (100.00%) | 3 / 3 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oesophageal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|----------------|---------------|---------------|
| Seborrhoeic keratosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aortic occlusion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Embolism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flushing | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vena cava embolism | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Axillary pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site pruritus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cyst | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 3 / 5 (60.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 2 | 3 | 1 |
| Feeling hot | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Inflammation | | | |

| | | | |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infusion site pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mass | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nodule | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Oedema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 2 | 0 | 1 |
| Pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 2 / 3 (66.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Secretion discharge | | | |

| | | | |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Temperature intolerance subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Immune system disorders Allergy to arthropod sting subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Contrast media reaction subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Reproductive system and breast disorders Breast mass subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Erectile dysfunction subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Galactorrhoea subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Pruritus genital subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Cough subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 5 (20.00%) 1 | 1 / 3 (33.33%) 1 |
| Dry throat subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |

| | | | |
|-----------------------------|----------------|----------------|---------------|
| Dysphonia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hiccups | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Laryngeal obstruction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lung disorder | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oropharyngeal discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--------------------------------|----------------|----------------|---------------|
| Painful respiration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paranasal sinus hypersecretion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rales | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Sneezing | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---------------------|---------------------|--------------------|
| Wheezing subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Psychiatric disorders | | | |
| Agitation subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Anxiety subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 1 / 5 (20.00%) 1 | 0 / 3 (0.00%) 0 |
| Confusional state subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Delirium subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Depression subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Insomnia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Mood altered subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Investigations | | | |
| Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Amylase decreased subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Amylase increased | | | |

| | | | |
|--|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 3 | 0 | 1 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood fibrinogen decreased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood iron decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood testosterone decreased | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urea increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urine present | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General physical condition abnormal | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 2 | 0 | 3 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |

| | | | |
|---|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procalcitonin increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Prothrombin time prolonged | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Serum ferritin decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tri-iodothyronine free abnormal | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eastern Cooperative Oncology Group performance status worsened | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|--------------------|---------------------|--------------------|
| Electrocardiogram QT prolonged subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Electrocardiogram T wave abnormal subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Influenza B virus test positive subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Anaemia postoperative subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Arthropod bite subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Chemical burn of skin subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Contusion subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Cystitis radiation subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Fall subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 5 (20.00%) 1 | 0 / 3 (0.00%) 0 |
| Humerus fracture subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Infusion related reaction subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Post procedural oedema | | | |

| | | | |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Radiation skin injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scratch | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sunburn | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|----------------|----------------|---------------|
| Palpitations | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial paralysis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Head discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperaesthesia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyposmia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lethargy | | | |

| | | | |
|--------------------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sensory disturbance | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|---------------------|---------------------|---------------------|
| Leukocytosis subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Lymphopenia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Neutropenia subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Ear and labyrinth disorders | | | |
| Ear discomfort subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 5 (20.00%) 1 | 1 / 3 (33.33%) 1 |
| Ear disorder subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Ear pain subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Hypoacusis subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Tinnitus subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Eye disorders | | | |
| Asthenopia subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Conjunctival haemorrhage subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Conjunctivitis allergic subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 5 (0.00%) 0 | 0 / 3 (0.00%) 0 |
| Diplopia | | | |

| | | | |
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| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry eye | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Episcleritis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye irritation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye pruritus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eyelid ptosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Keratitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lacrimation increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Periorbital swelling | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Photophobia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vision blurred | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal mass | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Ascites | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 5 (40.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |

| | | | |
|----------------------------------|----------------|----------------|---------------|
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 5 (40.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 3 | 3 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Duodenitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Epigastric discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Faeces soft | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingival pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-------------------------------|----------------|----------------|----------------|
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 3 | 1 | 1 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral disorder | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |

| | | | |
|--|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver disorder | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Diabetic foot | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ecchymosis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|----------------|----------------|----------------|
| Macule | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain of skin | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Papule | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Perioral dermatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Rash | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scar pain | | | |

| | | | |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin discolouration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin fissures | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitiligo | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Xeroderma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Micturition urgency | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nocturia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---------------|----------------|---------------|
| Proteinuria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal tubular necrosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urine abnormality | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercalcaemia of malignancy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 5 (40.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthritis | | | |

| | | | |
|---------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Back pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 5 (40.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Bone lesion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flank pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Limb discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Musculoskeletal stiffness | | | |

| | | | |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tendon disorder | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|----------------|----------------|---------------|
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Eye infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal fungal infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Kidney infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |

| | | | |
|-----------------------------------|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash pustular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 5 (20.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Acidosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 5 (20.00%) | 2 / 3 (66.67%) |
| occurrences (all) | 2 | 1 | 2 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|----------------|---------------|----------------|
| Hypermagnesaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 1 / 3 (33.33%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic alkalosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 5 (0.00%) | 0 / 3 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | MEDI0680 2.5 mg/kg Q2W + Durva 10 mg/kg Q2W | MEDI0680 10 mg/kg Q2W + Durva 10 mg/kg Q2W | MEDI0680 20 mg/kg Q2W + Durva 10 mg/kg Q2W |
|--|---|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 3 / 3 (100.00%) | 9 / 9 (100.00%) | 6 / 6 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oesophageal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seborrhoeic keratosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vascular disorders | | | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aortic occlusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Embolism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Flushing | | | |

| | | | |
|--|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 3 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vena cava embolism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Axillary pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site pruritus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cyst | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial pain | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 9 (22.22%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 2 | 3 |
| Feeling hot | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Inflammation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Infusion site pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Mass | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 3 |
| Nodule | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema | | | |

| | | | |
|--|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 9 (33.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 9 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 3 | 1 |
| Secretion discharge | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Temperature intolerance | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Immune system disorders | | | |
| Allergy to arthropod sting | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Contrast media reaction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Breast mass | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Erectile dysfunction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Galactorrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pruritus genital | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Cough | | | |
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 3 / 6 (50.00%) 4 |
| Dry throat | | | |
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Dysphonia | | | |
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Dyspnoea | | | |
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 2 / 9 (22.22%) 3 | 0 / 6 (0.00%) 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Epistaxis | | | |
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Haemoptysis | | | |
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hiccups | | | |
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Hypoxia | | | |
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Laryngeal obstruction | | | |

| | | | |
|--------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lung disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Oropharyngeal discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Painful respiration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paranasal sinus hypersecretion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rales | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis allergic | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 2 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sneezing | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper-airway cough syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Delirium | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|--------------------|---------------------|---------------------|
| Mood altered subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 6 (0.00%) 0 |
| Investigations | | | |
| Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 5 | 0 / 6 (0.00%) 0 |
| Amylase decreased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Amylase increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 1 / 6 (16.67%) 1 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 2 / 9 (22.22%) 4 | 0 / 6 (0.00%) 0 |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 6 (0.00%) 0 |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Blood creatine increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 2 / 9 (22.22%) 3 | 1 / 6 (16.67%) 1 |
| Blood fibrinogen decreased | | | |

| | | | |
|---|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood iron decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood testosterone decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urea increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood urine present | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General physical condition abnormal | | | |

| | | | |
|--|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procalcitonin increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Prothrombin time prolonged | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Serum ferritin decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tri-iodothyronine free abnormal | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |

| | | | |
|---|--------------------|--------------------|---------------------|
| Weight increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 1 / 6 (16.67%) 2 |
| White blood cell count increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Eastern Cooperative Oncology Group performance status worsened subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Electrocardiogram QT prolonged subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Electrocardiogram T wave abnormal subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Influenza B virus test positive subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Anaemia postoperative subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Arthropod bite subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Chemical burn of skin subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Contusion subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 2 / 6 (33.33%) 3 |
| Cystitis radiation | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fall | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 9 (11.11%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 1 | 2 |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post procedural oedema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Radiation skin injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Scratch | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sunburn | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wound | | | |

| | | | |
|--|--------------------|--------------------|--------------------|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 1 | 3 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Facial paralysis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Head discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |

| | | | |
|-------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 9 (22.22%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 3 | 0 |
| Hyperaesthesia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyposmia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sensory disturbance | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 3 / 9 (33.33%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 5 | 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Ear discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypoacusis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tinnitus | | | |

| | | | |
|--|--------------------|--------------------|--------------------|
| subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Eye disorders | | | |
| Asthenopia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctival haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis allergic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diplopia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry eye | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Episcleritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye irritation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Eye pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye pruritus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eyelid ptosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Keratitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|---------------|----------------|----------------|
| Lacrimation increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Periorbital swelling | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Photophobia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal mass | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain upper | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 0 | 2 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 3 / 9 (33.33%) | 5 / 6 (83.33%) |
| occurrences (all) | 0 | 12 | 5 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Duodenitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epigastric discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Faeces soft | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |

| | | | |
|----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingival pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 5 / 9 (55.56%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 7 | 3 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Pancreatitis | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 9 (22.22%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 2 | 2 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis acneiform | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diabetic foot | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Macule | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain of skin | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palmar-plantar erythrodysesthesia syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Papule | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Perioral dermatitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 5 / 9 (55.56%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 10 | 0 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Rash | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 4 / 9 (44.44%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 4 | 2 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scar pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin discolouration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin fissures | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vitiligo | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Xeroderma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|------------------------------|---------------|----------------|---------------|
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Micturition urgency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nocturia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Renal tubular necrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urine abnormality | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypercalcaemia of malignancy | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 9 (22.22%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 2 | 2 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Back pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 2 | 1 |
| Bone lesion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flank pain | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 9 (22.22%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 2 | 1 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Limb discomfort | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 1 | 4 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 9 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 0 | 2 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal pain | | | |

| | | | |
|-----------------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tendon disorder | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal fungal infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---------------|----------------|---------------|
| Influenza | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Kidney infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash pustular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory tract infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 9 (22.22%) | 3 / 6 (50.00%) |
| occurrences (all) | 1 | 3 | 4 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 9 (11.11%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Acidosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 2 | 4 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 9 (11.11%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |

| | | | |
|--|--------------------|---------------------|---------------------|
| Glucose tolerance impaired subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Gout subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hypercalcaemia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 1 / 6 (16.67%) 1 |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 6 (0.00%) 0 |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 3 | 0 / 6 (0.00%) 0 |
| Hypermagnesaemia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hypertriglyceridaemia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hyperuricaemia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 6 (0.00%) 0 |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 9 (11.11%) 1 | 0 / 6 (0.00%) 0 |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hypoglycaemia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 9 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hypokalaemia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 2 / 9 (22.22%) 4 | 0 / 6 (0.00%) 0 |

| | | | |
|-----------------------------|---------------|----------------|----------------|
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 2 / 9 (22.22%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 3 | 1 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic alkalosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 9 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | MEDI0680 20 mg/kg Q2W | MEDI0680 20 mg/kg Q2W + Durva 750 mg Q2W | Nivolumab 240mg Q2W |
|--|--------------------------|--|------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | 41 / 42 (97.62%) | 20 / 21 (95.24%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oesophageal adenocarcinoma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Seborrhoeic keratosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Vascular disorders | | | |

| | | | |
|--|----------------|-----------------|----------------|
| Aortic aneurysm | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Aortic occlusion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Embolism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flushing | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hot flush | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Hypertension | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 5 / 42 (11.90%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 7 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 42 (4.76%) | 1 / 21 (4.76%) |
| occurrences (all) | 1 | 2 | 1 |
| Vena cava embolism | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 5 / 42 (11.90%) | 1 / 21 (4.76%) |
| occurrences (all) | 1 | 7 | 1 |
| Axillary pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Catheter site pruritus | | | |

| | | | |
|-----------------------------|-----------------|------------------|-----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 42 (7.14%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 3 | 2 |
| Cyst | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Facial pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 4 / 4 (100.00%) | 19 / 42 (45.24%) | 6 / 21 (28.57%) |
| occurrences (all) | 4 | 25 | 7 |
| Feeling hot | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 2 |
| Inflammation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Infusion site pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Mass | | | |

| | | | |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Nodule | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Oedema | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 42 (2.38%) | 2 / 21 (9.52%) |
| occurrences (all) | 1 | 1 | 2 |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 5 / 42 (11.90%) | 3 / 21 (14.29%) |
| occurrences (all) | 1 | 7 | 4 |
| Pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 42 (7.14%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 4 (50.00%) | 8 / 42 (19.05%) | 2 / 21 (9.52%) |
| occurrences (all) | 2 | 12 | 3 |
| Secretion discharge | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Temperature intolerance | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Allergy to arthropod sting | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Contrast media reaction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|----------------|-----------------|-----------------|
| Reproductive system and breast disorders | | | |
| Breast mass | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erectile dysfunction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Galactorrhoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus genital | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Cough | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 9 / 42 (21.43%) | 8 / 21 (38.10%) |
| occurrences (all) | 2 | 17 | 9 |
| Dry throat | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 7 / 42 (16.67%) | 8 / 21 (38.10%) |
| occurrences (all) | 0 | 9 | 10 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 3 | 3 |

| | | | |
|--------------------------------|----------------|----------------|----------------|
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Hiccups | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Laryngeal obstruction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lung disorder | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 3 | 2 |
| Oropharyngeal discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 2 | 2 |
| Painful respiration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Paranasal sinus hypersecretion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 3 |

| | | | |
|---|--------------------|----------------------|---------------------|
| Productive cough subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 7 / 42 (16.67%) 8 | 2 / 21 (9.52%) 2 |
| Pulmonary haemorrhage subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 42 (0.00%) 0 | 1 / 21 (4.76%) 1 |
| Rales subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 42 (2.38%) 1 | 0 / 21 (0.00%) 0 |
| Rhinitis allergic subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 2 / 42 (4.76%) 2 | 0 / 21 (0.00%) 0 |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 4 / 42 (9.52%) 7 | 2 / 21 (9.52%) 4 |
| Sinus congestion subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 42 (2.38%) 1 | 0 / 21 (0.00%) 0 |
| Sneezing subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 2 / 42 (4.76%) 2 | 0 / 21 (0.00%) 0 |
| Upper-airway cough syndrome subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 42 (2.38%) 1 | 0 / 21 (0.00%) 0 |
| Wheezing subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 42 (2.38%) 1 | 0 / 21 (0.00%) 0 |
| Psychiatric disorders | | | |
| Agitation subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 42 (2.38%) 1 | 0 / 21 (0.00%) 0 |
| Anxiety subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 2 / 42 (4.76%) 2 | 2 / 21 (9.52%) 2 |
| Confusional state | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Delirium | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 2 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 5 / 42 (11.90%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 5 | 3 |
| Mood altered | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 42 (2.38%) | 3 / 21 (14.29%) |
| occurrences (all) | 1 | 3 | 3 |
| Amylase decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Amylase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 3 / 42 (7.14%) | 3 / 21 (14.29%) |
| occurrences (all) | 1 | 6 | 8 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 42 (4.76%) | 3 / 21 (14.29%) |
| occurrences (all) | 1 | 14 | 3 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood bilirubin increased | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood creatine increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 4 / 42 (9.52%) | 3 / 21 (14.29%) |
| occurrences (all) | 1 | 5 | 6 |
| Blood fibrinogen decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood iron decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood phosphorus decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood testosterone decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 2 | 2 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 3 |
| Blood urea increased | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood urine present | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General physical condition abnormal | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 4 / 42 (9.52%) | 2 / 21 (9.52%) |
| occurrences (all) | 2 | 19 | 12 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 2 |
| Platelet count increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Procalcitonin increased | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Prothrombin time prolonged | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Serum ferritin decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Tri-iodothyronine free abnormal | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 5 / 42 (11.90%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 7 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 42 (7.14%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| White blood cell count increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Eastern Cooperative Oncology Group performance status worsened | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Electrocardiogram T wave abnormal | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Influenza B virus test positive | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--|----------------|----------------|----------------|
| Injury, poisoning and procedural complications | | | |
| Anaemia postoperative | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Chemical burn of skin | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Contusion | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cystitis radiation | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 4 / 42 (9.52%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 4 | 1 |
| Post procedural oedema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Procedural pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Radiation skin injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rib fracture | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Scratch | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 42 (7.14%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 4 | 1 |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Sunburn | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Wound | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|-----------------------------|----------------|-----------------|-----------------|
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 3 / 42 (7.14%) | 4 / 21 (19.05%) |
| occurrences (all) | 3 | 3 | 4 |
| Dysgeusia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Facial paralysis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Head discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Headache | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 6 / 42 (14.29%) | 5 / 21 (23.81%) |
| occurrences (all) | 2 | 7 | 7 |
| Hyperaesthesia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Hyposmia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Neuropathy peripheral | | | |

| | | | |
|--------------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 5 / 42 (11.90%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 6 | 3 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 2 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sensory disturbance | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 42 (7.14%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 6 / 42 (14.29%) | 5 / 21 (23.81%) |
| occurrences (all) | 2 | 10 | 29 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphopenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Ear and labyrinth disorders | | | |
| Ear discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear disorder | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypoacusis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye disorders | | | |
| Asthenopia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctival haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Conjunctivitis allergic | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diplopia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dry eye | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Episcleritis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Eye irritation | | | |

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| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Eye pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Eye pruritus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Eyelid ptosis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Keratitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lacrimation increased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Periorbital swelling | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Photophobia | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 1 | 0 | 2 |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|---------------|------------------|-----------------|
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 42 (7.14%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Abdominal mass | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 4 / 42 (9.52%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 5 | 4 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 2 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 2 | 1 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 3 |
| Colitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 12 / 42 (28.57%) | 6 / 21 (28.57%) |
| occurrences (all) | 0 | 16 | 7 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 15 / 42 (35.71%) | 9 / 21 (42.86%) |
| occurrences (all) | 0 | 23 | 14 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 4 | 3 |
| Duodenitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|----------------------------------|---------------|----------------|-----------------|
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 1 | 5 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Epigastric discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Faeces soft | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 42 (7.14%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 1 | 2 |
| Gingival pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|----------------|------------------|-----------------|
| Nausea | | | |
| subjects affected / exposed | 3 / 4 (75.00%) | 10 / 42 (23.81%) | 7 / 21 (33.33%) |
| occurrences (all) | 4 | 13 | 8 |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral disorder | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 42 (7.14%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 2 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 11 / 42 (26.19%) | 6 / 21 (28.57%) |
| occurrences (all) | 1 | 15 | 8 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Liver disorder | | | |

| | | | |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 42 (2.38%) 1 | 0 / 21 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 1 | 0 | 2 |
| Diabetic foot | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 5 / 42 (11.90%) | 4 / 21 (19.05%) |
| occurrences (all) | 0 | 5 | 4 |
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 4 |
| Macule | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 3 / 42 (7.14%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Pain of skin | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|----------------|-----------------|-----------------|
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Papule | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Perioral dermatitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 7 / 42 (16.67%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 10 | 4 |
| Rash | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 7 / 42 (16.67%) | 4 / 21 (19.05%) |
| occurrences (all) | 0 | 9 | 4 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 4 / 21 (19.05%) |
| occurrences (all) | 0 | 5 | 5 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Scar pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin discolouration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin fissures | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin lesion | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 4 (25.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 2 | 1 | 1 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitiligo | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Xeroderma | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 2 | 2 |
| Micturition urgency | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nocturia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 2 | 2 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal tubular necrosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|--|---------------------|------------------------|-----------------------|
| Urinary retention subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 42 (2.38%) 1 | 0 / 21 (0.00%) 0 |
| Urinary tract pain subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 42 (0.00%) 0 | 1 / 21 (4.76%) 1 |
| Urine abnormality subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 42 (2.38%) 1 | 0 / 21 (0.00%) 0 |
| Endocrine disorders | | | |
| Adrenal insufficiency subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 1 / 42 (2.38%) 2 | 0 / 21 (0.00%) 0 |
| Hypercalcaemia of malignancy subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 42 (2.38%) 4 | 0 / 21 (0.00%) 0 |
| Hyperthyroidism subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 1 / 42 (2.38%) 1 | 1 / 21 (4.76%) 1 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 4 / 42 (9.52%) 4 | 2 / 21 (9.52%) 2 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 10 / 42 (23.81%) 18 | 7 / 21 (33.33%) 12 |
| Arthritis subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 42 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Back pain subjects affected / exposed occurrences (all) | 1 / 4 (25.00%) 1 | 10 / 42 (23.81%) 11 | 2 / 21 (9.52%) 2 |
| Bone lesion subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 1 / 42 (2.38%) 1 | 0 / 21 (0.00%) 0 |
| Flank pain | | | |

| | | | |
|---------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 4 / 42 (9.52%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 5 | 1 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Limb discomfort | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 6 / 42 (14.29%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 6 | 2 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 1 | 3 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 4 / 42 (9.52%) | 1 / 21 (4.76%) |
| occurrences (all) | 1 | 6 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 5 / 42 (11.90%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 6 | 1 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 6 / 42 (14.29%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 9 | 3 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Osteoarthritis | | | |

| | | | |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 6 / 42 (14.29%) | 4 / 21 (19.05%) |
| occurrences (all) | 0 | 7 | 5 |
| Pain in jaw | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tendon disorder | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---------------|----------------|----------------|
| Gastrointestinal fungal infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Kidney infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Lower respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 42 (7.14%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Oral candidiasis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral herpes | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash pustular | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 2 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 0 | 3 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Tooth infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 42 (7.14%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 5 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 4 (25.00%) | 2 / 42 (4.76%) | 4 / 21 (19.05%) |
| occurrences (all) | 1 | 2 | 5 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Viral upper respiratory tract infection | | | |

| | | | |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 4 (0.00%) 0 | 0 / 42 (0.00%) 0 | 0 / 21 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Acidosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 5 / 42 (11.90%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 5 | 1 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 3 | 2 |
| Glucose tolerance impaired | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 1 | 1 |
| Gout | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 6 / 42 (14.29%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 9 | 2 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 3 | 5 |
| Hypermagnesaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|-----------------------------|---------------|-----------------|-----------------|
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 2 / 42 (4.76%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 5 / 42 (11.90%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 6 | 2 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 4 / 42 (9.52%) | 2 / 21 (9.52%) |
| occurrences (all) | 0 | 9 | 6 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 3 / 42 (7.14%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 4 | 5 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 3 / 21 (14.29%) |
| occurrences (all) | 0 | 1 | 8 |
| Metabolic alkalosis | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 0 / 42 (0.00%) | 1 / 21 (4.76%) |
| occurrences (all) | 0 | 0 | 1 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 4 (0.00%) | 1 / 42 (2.38%) | 0 / 21 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 16 April 2014 | Name AMP 514 was replaced with MEDI0680. Specified that immunotherapy-naïve and pretreated participants were to be enrolled in up to 8 hematologic and solid tumor cohorts and that the immunotherapy naïve and pretreated cohorts could enroll an additional 60 participants based on emerging efficacy and safety data from the current study and ongoing studies. Specified that each hematologic cohort, including MDS, would only be expanded after submission of a formal protocol amendment. Updated the inclusion criteria to include NSCLC participants must have failed to respond or relapsed following platinum containing doublet chemotherapy. |
| 01 October 2014 | To align with strategy of study focus the tumor types were limited to non-small cell lung cancer, squamous cell carcinoma of the head and neck, microsatellite instability-high colorectal cancer, bladder cancer, ovarian cancer, esophageal cancer, gastric cancer, and renal cell carcinoma in the dose-escalation phase. Added 20 mg/kg MEDI0680 plus 10 mg/kg durvalumab cohort to the Q2W dose-escalation schedule. Revised the dose-escalation phase to allow for any dose-escalation cohort that has not exceeded the MTD to be expanded by up to a maximum of 18 participants. Updated the inclusion criteria as: Revised to reflect the solid tumor types that would be allowed in the dose escalation phase. Indicated that no more than 3 prior lines of systemic therapy would be allowed in the recurrent or metastatic setting; added specific inclusion criteria for NSCLC participants in dose-escalation and dose-expansion; and added that participants with previously treated CNS metastases must be radiographically and neurologically stable for at least 6 weeks. |
| 11 February 2016 | Dose-expansion phase updated to enroll PD-L1 positive immunotherapy-naïve participants with RCC, added MEDI0680 monotherapy as a comparator arm; revised primary objective to evaluate antitumor activity based on investigator assessed response and secondary objectives to describe safety and tolerability, and to evaluate antitumor activity based on BICR assessed response in immunotherapy-naïve participants with advanced or metastatic ccRCC. Removed exploratory objective on patient reported outcomes. Replaced primary endpoint of maximum tolerated dose with presence of AEs, SAEs, laboratory parameters, vital signs, physical examinations, and ECG results. Added endpoint of PD-L1 expression/localization on tumor membrane and tumor infiltrating immune cells within tumor microenvironment. Increased sample size to 156 and study centers to 80. Participants in dose expansion phase were not to be replaced. Updated safety assessment. Added Appendix of Dose Modifications for Toxicity Management. |
| 27 May 2016 | Revised the exclusion criteria to permit enrollment of participants with prior endocrine toxicities who are stable on replacement therapy. |
| 29 March 2017 | Removed MEDI0680 monotherapy arm in the dose-expansion phase and replaced with a nivolumab monotherapy arm. Clarified that OR is the primary endpoint and that OS is a secondary endpoint in the dose expansion phase. Reduced the planned sample size from 156 to approximately 96 participants for both dose-escalation and dose-expansion phases; from 120 to approximately 60 in dose-expansion phases; and study center numbers from 80 to 50. Added an interim futility analysis for the MEDI0680/durvalumab combination therapy arm in the dose-expansion phase after 20 participants have been randomized and have reached their second post baseline disease assessment or have completed the study. Changed the randomization ratio of combination and monotherapy from 1:1 to 2:1. Revised end of study definition from 3 years to 2 years after the last participant was enrolled and added possible treatment options for participants still receiving treatment at the end of the study. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|---|
| Study did not meet primary endpoint, so, BICR data for antitumor activity were not collected. Numeric data were not collected for "Change from baseline in target lesion" as it was to be analysed by Spider plots per Statistical Analysis Plan. |
|---|

Notes: