



Clinical trial results:

A randomized, double-blind, placebo-controlled, phase III study comparing the combination of PDR001, dabrafenib and trametinib versus placebo, dabrafenib and trametinib in previously untreated patients with unresectable or metastatic BRAF V600 mutant melanoma
Summary

| | |
|--------------------------|--|
| EudraCT number | 2016-002794-35 |
| Trial protocol | DE SE GB ES AT CZ PL BG GR BE PT NL DK HU IT |
| Global end of trial date | 21 August 2024 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 |
| This version publication date | 27 August 2025 |
| First version publication date | 27 August 2025 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | CPDR001F2301 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02967692 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Novartis Pharma AG |
| Sponsor organisation address | Lichtstrasse 35, Basel, Switzerland, 4056 |
| Public contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com |
| Scientific contact | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.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 | 21 August 2024 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 21 August 2024 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate safety and efficacy of the combination of an anti-PD-1 antibody (PDR001), a BRAF inhibitor (dabrafenib) and a MEK inhibitor (trametinib) in patients with BRAF V600 mutant, unresectable and metastatic melanoma.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 17 February 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Argentina: 11 |
| Country: Number of subjects enrolled | Australia: 14 |
| Country: Number of subjects enrolled | Austria: 11 |
| Country: Number of subjects enrolled | Belgium: 4 |
| Country: Number of subjects enrolled | Brazil: 9 |
| Country: Number of subjects enrolled | Bulgaria: 9 |
| Country: Number of subjects enrolled | Canada: 7 |
| Country: Number of subjects enrolled | Chile: 18 |
| Country: Number of subjects enrolled | Czechia: 19 |
| Country: Number of subjects enrolled | Denmark: 1 |
| Country: Number of subjects enrolled | France: 92 |
| Country: Number of subjects enrolled | Germany: 66 |
| Country: Number of subjects enrolled | United Kingdom: 28 |
| Country: Number of subjects enrolled | Greece: 10 |
| Country: Number of subjects enrolled | Hungary: 10 |
| Country: Number of subjects enrolled | Israel: 10 |
| Country: Number of subjects enrolled | Italy: 83 |
| Country: Number of subjects enrolled | Japan: 10 |
| Country: Number of subjects enrolled | Mexico: 3 |

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Netherlands: 8 |
| Country: Number of subjects enrolled | Norway: 6 |
| Country: Number of subjects enrolled | Poland: 14 |
| Country: Number of subjects enrolled | Portugal: 3 |
| Country: Number of subjects enrolled | Russian Federation: 51 |
| Country: Number of subjects enrolled | Spain: 34 |
| Country: Number of subjects enrolled | Sweden: 6 |
| Country: Number of subjects enrolled | Switzerland: 13 |
| Country: Number of subjects enrolled | Thailand: 2 |
| Country: Number of subjects enrolled | United States: 16 |
| Worldwide total number of subjects | 568 |
| EEA total number of subjects | 376 |

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) | 409 |
| From 65 to 84 years | 157 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details:

Part 1 and 2 were conducted in 18 centers across 12 countries. Part 3 is conducted in 190 centers across 29 countries

Pre-assignment

Screening details:

The screening phase began once written informed consent was provided and ended after 28 days or when subject received the first dose (Part 1 and 2) or was randomized (Part 3), whichever came first.

Period 1

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

Arms

| | |
|------------------------------|---|
| Are arms mutually exclusive? | Yes |
| Arm title | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD |

Arm description:

In Part 1, participants are treated with Spartalizumab (PDR001) 400 mg Q4W in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD).

| | |
|--|----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Spartalizumab |
| Investigational medicinal product code | |
| Other name | PDR001 |
| Pharmaceutical forms | Powder for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Spartalizumab powder for solution is used in Part 1 and Part 2, and as concentrate for solution for infusion for Part 3. Spartalizumab is administered via intravenous infusion over 30 minutes once every 4 weeks

| | |
|--|------------|
| Investigational medicinal product name | Trametinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Trametinib 2 mg tablets QD is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions

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

Dosage and administration details:

Dabrafenib 150 mg capsules BID is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions.

| | |
|------------------|--|
| Arm title | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD |
|------------------|--|

Arm description:

In Part 2, participants are treated with Spartalizumab (PDR001) 400 mg Q4W in combination with the

approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD).

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Spartalizumab |
| Investigational medicinal product code | |
| Other name | PDR001 |
| Pharmaceutical forms | Powder for solution for infusion, Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Spartalizumab powder for solution is used in Part 1 and Part 2, and as concentrate for solution for infusion for Part 3. Spartalizumab is administered via intravenous infusion over 30 minutes once every 4 weeks

| | |
|--|------------|
| Investigational medicinal product name | Trametinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Trametinib 2 mg tablets QD is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions

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

Dosage and administration details:

Dabrafenib 150 mg capsules BID is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions.

| | |
|------------------|---|
| Arm title | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD |
|------------------|---|

Arm description:

In Part 3, participants are randomized to receive Spartalizumab (PDR001) at the RP3R identified in Part 1 (400 mg Q4W) in combination with approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD)

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Spartalizumab |
| Investigational medicinal product code | |
| Other name | PDR001 |
| Pharmaceutical forms | Powder for solution for infusion, Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Spartalizumab powder for solution is used in Part 1 and Part 2, and as concentrate for solution for infusion for Part 3. Spartalizumab is administered via intravenous infusion over 30 minutes once every 4 weeks

| | |
|--|------------|
| Investigational medicinal product name | Trametinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Trametinib 2 mg tablets QD is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions

| | |
|--|------------|
| Investigational medicinal product name | Dabrafenib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |

| | |
|--------------------------|----------|
| Routes of administration | Oral use |
|--------------------------|----------|

Dosage and administration details:

Dabrafenib 150 mg capsules BID is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions.

| | |
|------------------|--|
| Arm title | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
|------------------|--|

Arm description:

In Part 3, participants are randomized to receive matching placebo in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD)

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

Dosage and administration details:

Dabrafenib 150 mg capsules BID is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions.

| | |
|--|---|
| Investigational medicinal product name | Spartalizumab matching placebo |
| Investigational medicinal product code | |
| Other name | Placebo |
| Pharmaceutical forms | Powder for solution for infusion, Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Spartalizumab matching placebo is used as concentrate for solution for infusion for Part 3.

Spartalizumab matching placebo is administered via intravenous infusion over 30 minutes once every 4 weeks

| | |
|--|------------|
| Investigational medicinal product name | Trametinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Trametinib 2 mg tablets QD is administered orally for Days 1-28 of a 28-day cycle, in fasting conditions

| Number of subjects in period 1 | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD |
|---------------------------------------|---|--|---|
| Started | 9 | 27 | 267 |
| Treated | 9 | 27 | 267 |
| Completed | 0 | 0 | 0 |
| Not completed | 9 | 27 | 267 |
| Adverse event, serious fatal | - | 1 | 13 |
| Physician decision | - | - | 22 |
| Adverse event, non-fatal | 2 | 9 | 60 |
| Protocol deviation | 1 | - | 1 |

| | | | |
|-----------------------------|---|----|-----|
| Study terminated by sponsor | 2 | 1 | 42 |
| Progressive disease | 3 | 15 | 114 |
| Lost to follow-up | - | - | 1 |
| Subject/guardian decision | 1 | 1 | 14 |

| Number of subjects in period 1 | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
|---------------------------------------|---|
| Started | 265 |
| Treated | 264 |
| Completed | 0 |
| Not completed | 265 |
| Adverse event, serious fatal | 13 |
| Physician decision | 13 |
| Adverse event, non-fatal | 28 |
| Protocol deviation | 1 |
| Study terminated by sponsor | 37 |
| Progressive disease | 151 |
| Lost to follow-up | - |
| Subject/guardian decision | 22 |

Baseline characteristics

Reporting groups

| | |
|--|--|
| Reporting group title | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD |
| Reporting group description: In Part 1, participants are treated with Spartalizumab (PDR001) 400 mg Q4W in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD). | |
| Reporting group title | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD |
| Reporting group description: In Part 2, participants are treated with Spartalizumab (PDR001) 400 mg Q4W in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD). | |
| Reporting group title | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD |
| Reporting group description: In Part 3, participants are randomized to receive Spartalizumab (PDR001) at the RP3R identified in Part 1 (400 mg Q4W) in combination with approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD) | |
| Reporting group title | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
| Reporting group description: In Part 3, participants are randomized to receive matching placebo in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD) | |

| Reporting group values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD |
|---|---|--|---|
| Number of subjects | 9 | 27 | 267 |
| Age Categorical Units: Participants | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 7 | 18 | 189 |
| >=65 years | 2 | 9 | 78 |
| Sex: Female, Male Units: Participants | | | |
| Female | 2 | 12 | 119 |
| Male | 7 | 15 | 148 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| White | 9 | 24 | 225 |
| Asian | 0 | 2 | 5 |
| Other | 0 | 1 | 15 |
| Unknown | 0 | 0 | 22 |

| Reporting group values | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD | Total | |
|--|--|-------|--|
| Number of subjects | 265 | 568 | |
| Age Categorical Units: Participants | | | |
| <=18 years | 0 | 0 | |
| Between 18 and 65 years | 195 | 409 | |

| | | | |
|------------|----|-----|--|
| >=65 years | 70 | 159 | |
|------------|----|-----|--|

| | | | |
|---|-----|-----|--|
| Sex: Female, Male Units: Participants | | | |
| Female | 106 | 239 | |
| Male | 159 | 329 | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| White | 227 | 485 | |
| Asian | 5 | 12 | |
| Other | 14 | 30 | |
| Unknown | 19 | 41 | |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD |
| Reporting group description: In Part 1, participants are treated with Spartalizumab (PDR001) 400 mg Q4W in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD). | |
| Reporting group title | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD |
| Reporting group description: In Part 2, participants are treated with Spartalizumab (PDR001) 400 mg Q4W in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD). | |
| Reporting group title | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD |
| Reporting group description: In Part 3, participants are randomized to receive Spartalizumab (PDR001) at the RP3R identified in Part 1 (400 mg Q4W) in combination with approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD) | |
| Reporting group title | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
| Reporting group description: In Part 3, participants are randomized to receive matching placebo in combination with the approved dose of dabrafenib (150 mg BID) and trametinib (2 mg QD) | |

Primary: Safety Run-In (Part 1): Number of participants with dose limiting toxicities (DLTs)

| | |
|---|---|
| End point title | Safety Run-In (Part 1): Number of participants with dose limiting toxicities (DLTs) ^{[1][2]} |
| End point description: DLT was defined as an adverse event or abnormal laboratory value that was unrelated to disease, disease progression, inter-current illness, or concomitant medications and occurred within 8 weeks of treatment with spartalizumab in combination with dabrafenib and trametinib. The DLT criteria included Grade 4 hematological adverse events, Grade 4 bilirubin elevation, specific gastrointestinal adverse events, symptomatic serum amylase or lipase elevation, Grade 3 or higher hypertension, Grade 3 or higher cardiac events, Grade 2 or higher pneumonitis, Grade 3 or higher immune-related toxicities, infusion-related reactions, other clinically significant adverse events, and toxicities leading to a dosing delay of over 12 weeks. NCI CTCAE v4.03 was used for grading DLTs | |
| End point type | Primary |
| End point timeframe: Up to 8 weeks (Part 1) | |

Notes:

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

Justification: Only descriptive statistics performed

[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 applicable to Part 1 Arm

| | | | | |
|-----------------------------|---|--|--|--|
| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 | | | |
| Units: Participants | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Biomarker cohort (Part 2): Change from baseline in programmed cell death-ligand 1 (PD-L1) expression upon treatment with spartalizumab in combination with dabrafenib and trametinib

| | |
|-----------------|--|
| End point title | Biomarker cohort (Part 2): Change from baseline in programmed cell death-ligand 1 (PD-L1) expression upon treatment with spartalizumab in combination with dabrafenib and trametinib ^[3] ^[4] |
|-----------------|--|

End point description:

Change from baseline in PD-L1 expression (as determined by immunohistochemistry in tissue samples) upon treatment with spartalizumab in combination with dabrafenib and trametinib in participants from Part 2

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

End point timeframe:

Baseline, Cycle 1 Day 15 and Cycle 3 Day 1 (Part 2). Each cycle is 28 days

Notes:

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

Justification: Only descriptive statistics performed

[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 applicable to Part 2 Arm

| | | | | |
|---|--|--|--|--|
| End point values | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 9 | | | |
| Units: Percentage of positive tumor cells | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 15 | 1.7 (± 13.05) | | | |
| Cycle 3 Day 1 | 2.7 (± 7.63) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Biomarker cohort (Part 2): Change from baseline in CD8+ cells upon treatment with spartalizumab in combination with dabrafenib and trametinib

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|-----------------|---|
| End point title | Biomarker cohort (Part 2): Change from baseline in CD8+ cells upon treatment with spartalizumab in combination with dabrafenib and trametinib ^[5] ^[6] |
|-----------------|---|

End point description:

Change from baseline in CD8+ cells (as determined by flow cytometry in blood samples) upon treatment with spartalizumab in combination with dabrafenib and trametinib in participants from Part 2

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

End point timeframe:

Baseline, Cycle 1 Day 15 and Cycle 3 Day 1 (Part 2). Each cycle is 28 days

Notes:

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

Justification: Only descriptive statistics performed

[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 applicable to Part 2 Arm

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: Percentage Marker Area | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 15 | 0.4 (± 3.22) | | | |
| Cycle 3 Day 1 | 1.2 (± 2.43) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Randomized (Part 3): Progression-Free Survival (PFS) as per investigator's assessment by RECIST 1.1

| | |
|-----------------|--|
| End point title | Randomized (Part 3): Progression-Free Survival (PFS) as per investigator's assessment by RECIST 1.1 ^[7] |
|-----------------|--|

End point description:

Progression-free survival was defined as the time from the date of first dose to the date of the first documented radiological progression per investigator's assessment according to RECIST 1.1 or death due to any cause. The distribution of PFS was estimated using the Kaplan-Meier (KM) method. If a patient had not had an event at the time of data cut-off, progression-free survival was censored at the date of last adequate tumor assessment.

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

End point timeframe:

Up to disease progression or death due to any cause, whichever occurs first, assessed up to 2.8 years (Part 3)

Notes:

[7] - 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 applicable to Part 3-Arm 1 and Part 3-Arm 2

| | | | | |
|----------------------------------|---|---|--|--|
| End point values | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 267 | 265 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 16.2 (12.7 to 23.9) | 12.0 (10.2 to 15.4) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | P3: PFS per inv. assessment (RECIST 1.1) |
| Comparison groups | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD v P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
| Number of subjects included in analysis | 532 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.042 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.82 |
| Confidence interval | |
| level | Other: 2 % |
| sides | 2-sided |
| lower limit | 0.655 |
| upper limit | 1.027 |

Secondary: Overall survival (OS)

| | |
|---|-----------------------|
| End point title | Overall survival (OS) |
| End point description: | |
| Overall survival was defined as the time from date of randomization to date of death due to any cause | |
| End point type | Secondary |
| End point timeframe: | |
| Up to death due to any cause, assessed up to approximately 7 years | |

| | | | | |
|----------------------------------|---|--|---|---|
| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 27 | 267 | 265 |
| Units: Months | | | | |
| median (confidence interval 95%) | 999 (12.2 to 999) | 30.7 (21.3 to 67.4) | 61.5 (41.6 to 999) | 41.6 (30.6 to 56.9) |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate (ORR) as per investigator's assessment by RECIST 1.1

| | |
|-----------------|--|
| End point title | Overall response rate (ORR) as per investigator's assessment by RECIST 1.1 |
|-----------------|--|

End point description:

ORR was defined as the percentage of subjects with confirmed best overall response of complete response (CR) or partial response (PR), as per investigator's assessment by RECIST 1.1. CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to <10 mm PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters

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

End point timeframe:

Part 1: Up to 3.3 years. Part 2: Up to 3 years. Part 3: Up to 2.8 years

| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
|-----------------------------------|---|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 27 | 267 | 265 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 100.0 (66.4 to 100.0) | 70.4 (49.8 to 86.2) | 68.5 (62.6 to 74.1) | 64.2 (58.1 to 69.9) |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR) as per investigator's assessment by RECIST 1.1

| | |
|-----------------|---|
| End point title | Duration of response (DOR) as per investigator's assessment by RECIST 1.1 |
|-----------------|---|

End point description:

DOR was defined as the time from first documented response of CR or PR to date of first documented progression or death, according to RECIST 1.1 criteria. The distribution of DOR was estimated using the KM method. CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to <10 mm PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters

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

End point timeframe:

From first documented response to date of first documented progression or death, up to 3.3 years (Part 1), 3 years (Part 2) and 2.8 years (Part 3)

| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
|----------------------------------|---|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 19 | 183 | 170 |
| Units: Months | | | | |
| median (confidence interval 95%) | 999 (8.3 to 999) | 20.0 (9.4 to 999) | 999 (18.6 to 999) | 20.7 (13.0 to 999) |

Statistical analyses

No statistical analyses for this end point

Secondary: Disease control rate (DCR) as per investigator's assessment by RECIST 1.1

| | |
|-----------------|---|
| End point title | Disease control rate (DCR) as per investigator's assessment by RECIST 1.1 |
|-----------------|---|

End point description:

DCR was defined as the percentage of participants with CR or PR or subjects with stable disease (SD) lasting for a duration of at least 24 weeks as per local review according to RECIST 1.1 criteria. CR: Disappearance of all non-nodal target lesions. In addition, any pathological lymph nodes assigned as target lesions must have a reduction in short axis to <10 mm PR: At least a 30% decrease in the sum of diameter of all target lesions, taking as reference the baseline sum of diameters SD: Neither sufficient shrinkage to qualify for PR or CR nor an increase in lesions which would qualify for progressive disease.

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

End point timeframe:

Part 1: Up to 3.3 years. Part 2: Up to 3 years. Part 3: Up to 2.8 year

| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
|-----------------------------------|---|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 27 | 267 | 265 |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 100.0 (66.4 to 100.0) | 92.6 (75.7 to 99.1) | 84.3 (79.3 to 88.4) | 86.4 (81.7 to 90.3) |

Statistical analyses

Secondary: Randomized (Part 3): Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Global health status scores

| | |
|-----------------|---|
| End point title | Randomized (Part 3): Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Global health status scores ^[8] |
|-----------------|---|

End point description:

The EORTC QLQ-C30 was a 30-item questionnaire that patients complete, consisting of both multi-item scales and single-item measures. It included five functional scales, three symptom scales, six single items, and a Global Health Status/Quality of Life (GHS/QoL) scale. The GHS/QoL scale had seven possible response scores ranging from 1 (very poor) to 7 (excellent), which were averaged and transformed to a 0-100 scale. A higher score on this scale indicated a better quality of life. The change from baseline in GHS/QoL scores was calculated. A positive change from baseline indicated improvement in the patient's quality of life.

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

End point timeframe:

From baseline to 60 days post progression, assessed up to 2.8 years (Part 3)

Notes:

[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 applicable to Part 3-Arm 1 and Part 3-Arm 2

| End point values | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 186 | | |
| Units: Score on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 4 Day 1 | 0.81 (± 19.300) | 2.20 (± 24.918) | | |
| Cycle 6 Day 1 | 1.22 (± 25.050) | 1.90 (± 21.197) | | |
| Cycle 8 Day 1 | 0.00 (± 24.526) | 0.50 (± 19.608) | | |
| Cycle 10 Day 1 | 1.88 (± 23.088) | 0.27 (± 18.752) | | |
| Cycle 12 Day 1 | 0.61 (± 25.906) | 0.00 (± 24.541) | | |
| Cycle 14 Day 1 | 0.65 (± 23.561) | -0.89 (± 23.306) | | |
| Cycle 16 Day 1 | 0.82 (± 25.186) | 1.76 (± 24.142) | | |
| Cycle 18 Day 1 | -0.46 (± 24.106) | -0.10 (± 19.193) | | |
| Cycle 20 Day 1 | 1.93 (± 21.766) | -1.02 (± 23.144) | | |
| Cycle 22 Day 1 | 0.95 (± 22.047) | 2.29 (± 21.947) | | |
| Cycle 25 Day 1 | 3.57 (± 23.981) | -0.24 (± 25.497) | | |
| Cycle 28 Day 1 | 4.50 (± 19.793) | 1.06 (± 22.513) | | |
| Cycle 31 Day 1 | 11.59 (± 24.967) | 6.73 (± 21.084) | | |

| | | | | |
|--------------------------|----------------------|----------------------|--|--|
| Cycle 34 Day 1 | 16.67 (± 47.140) | 13.89 (± 20.184) | | |
| 30 days post-progression | -11.59 (± 24.967) | -7.78 (± 29.274) | | |
| 60 days post-progression | -11.54 (± 16.506) | -17.19 (± 24.050) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized (Part 3): Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Physical functioning scale scores

| | |
|-----------------|---|
| End point title | Randomized (Part 3): Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Physical functioning scale scores ^[9] |
|-----------------|---|

End point description:

The EORTC QLQ-C30 was a patient completed 30 item questionnaire that was composed of both multi-item scales and single-item measures. These included five functional scales, three symptom scales, six single items and a global health status/QoL scale. The EORTC QLQ-C30 physical functioning scale measured a patient's ability to carry out daily activities and tasks requiring physical exertion. It consisted of five questions asking patients to rate their level of physical functioning, with response options ranging from 1="not at all" to 4="very much". The scores for each item were summed and transformed to a 0 to 100 scale, with higher scores indicating better physical functioning. The change from baseline in physical functioning scale scores was calculated. A positive change from baseline indicated improvement in physical functioning.

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

End point timeframe:

From baseline to 60 days post progression, assessed up to 2.8 years (Part 3)

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 applicable to Part 3-Arm 1 and Part 3-Arm 2

| End point values | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 186 | | |
| Units: Score on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 4 Day 1 | -1.52 (± 16.243) | -0.70 (± 17.618) | | |
| Cycle 6 Day 1 | -2.38 (± 16.121) | -0.60 (± 14.824) | | |
| Cycle 8 Day 1 | -1.29 (± 18.350) | -0.59 (± 15.687) | | |
| Cycle 10 Day 1 | -0.18 (± 17.985) | -1.11 (± 13.736) | | |
| Cycle 12 Day 1 | -1.39 (± 18.108) | -0.85 (± 10.652) | | |
| Cycle 14 Day 1 | -2.42 (± 16.720) | -2.61 (± 12.320) | | |

| | | | | |
|--------------------------|-------------------|-------------------|--|--|
| Cycle 16 Day 1 | -4.19 (± 20.301) | -2.24 (± 13.331) | | |
| Cycle 18 Day 1 | -3.48 (± 18.862) | -3.55 (± 13.474) | | |
| Cycle 20 Day 1 | -4.07 (± 15.316) | -1.73 (± 11.536) | | |
| Cycle 22 Day 1 | -3.21 (± 15.538) | -0.85 (± 11.157) | | |
| Cycle 25 Day 1 | -1.35 (± 16.510) | -2.67 (± 13.158) | | |
| Cycle 28 Day 1 | -0.80 (± 13.843) | -2.67 (± 15.953) | | |
| Cycle 31 Day 1 | -2.03 (± 10.719) | -1.79 (± 9.533) | | |
| Cycle 34 Day 1 | 0.00 (± 0.000) | -3.33 (± 5.578) | | |
| 30 days post-progression | -6.67 (± 18.641) | -8.67 (± 19.973) | | |
| 60 days post-progression | -13.85 (± 15.977) | -21.25 (± 27.991) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized (Part 3): Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Pain symptom scale scores

| | |
|-----------------|--|
| End point title | Randomized (Part 3): Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Pain symptom scale scores ^[10] |
|-----------------|--|

End point description:

The EORTC QLQ-C30 was a patient completed 30 item questionnaire that was composed of both multi-item scales and single-item measures. These included five functional scales, three symptom scales, six single items and a global health status/QoL scale. The EORTC QLQ-C30 pain symptom scale was one of the symptom scales in the questionnaire, which measured the severity of pain experienced by the patient. The pain symptom scale consisted of two items, one measuring the severity of pain and the other measuring the use of painkillers. The items were rated on a 4-point scale ranging from 1="not at all" to 4="very much". The scores for each item were summed and transformed to a 0 to 100 scale, with higher scores indicating more severe pain. The change from baseline in pain symptom scale scores was calculated. A negative change from baseline indicated improvement.

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

End point timeframe:

From baseline to 60 days post progression, assessed up to 2.8 years (Part 3)

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 applicable to Part 3-Arm 1 and Part 3-Arm 2

| End point values | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 175 | 186 | | |
| Units: Score on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 4 Day 1 | -5.24 (± 26.434) | -5.29 (± 24.881) | | |
| Cycle 6 Day 1 | -6.43 (± 28.820) | -7.49 (± 23.611) | | |
| Cycle 8 Day 1 | -4.91 (± 29.176) | -4.11 (± 24.420) | | |
| Cycle 10 Day 1 | -7.95 (± 28.346) | -4.76 (± 23.557) | | |
| Cycle 12 Day 1 | -8.33 (± 28.890) | -5.26 (± 22.646) | | |
| Cycle 14 Day 1 | -5.50 (± 28.140) | -3.56 (± 23.062) | | |
| Cycle 16 Day 1 | -5.86 (± 26.220) | -4.44 (± 25.820) | | |
| Cycle 18 Day 1 | -3.15 (± 30.178) | -3.21 (± 20.898) | | |
| Cycle 20 Day 1 | -4.47 (± 30.659) | -2.85 (± 23.249) | | |
| Cycle 22 Day 1 | -5.49 (± 27.049) | -3.54 (± 23.969) | | |
| Cycle 25 Day 1 | -6.25 (± 28.868) | -4.76 (± 20.685) | | |
| Cycle 28 Day 1 | -3.00 (± 26.872) | -3.03 (± 22.701) | | |
| Cycle 31 Day 1 | -10.14 (± 24.995) | -7.05 (± 34.696) | | |
| Cycle 34 Day 1 | -8.33 (± 11.785) | -5.56 (± 8.607) | | |
| 30 days post-progression | 9.42 (± 28.791) | 0.56 (± 28.190) | | |
| 60 days post-progression | 15.38 (± 19.792) | 11.46 (± 24.884) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized (Part 3): Time to 10 point definitive deterioration in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Global Health Status

| | |
|-----------------|--|
| End point title | Randomized (Part 3): Time to 10 point definitive deterioration in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) C30- Global Health Status ^[11] |
|-----------------|--|

End point description:

The EORTC QLQ-C30 was a patient completed 30 item questionnaire that was composed of both multi-item scales and single-item measures. These included five functional scales, three symptom scales, six single items and a global health status/QoL scale. The GHS/QoL scale had seven possible response scores ranging from 1 (very poor) to 7 (excellent), which were averaged and transformed to a 0-100

scale. A higher score on this scale indicated a better quality of life. The time to definitive 10 point deterioration is defined as the time from the date of randomization to the date of event, which is defined as at least 10 points relative to baseline worsening of the GHS/QoL score or death due to any cause. If a subject had not had an event, the time to deterioration was censored at the date of the last adequate assessment. The distribution was estimated using KM method.

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

End point timeframe:

From baseline to date of at least 10 points relative to baseline worsening of the global health status score or death due to any cause, up to 2.8 years (Part 3)

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 applicable to Part 3-Arm 1 and Part 3-Arm 2

| End point values | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD | | |
|----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 267 | 265 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 19.4 (15.7 to 24.9) | 22.1 (17.5 to 999) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | P3: Time to 10pt def. det. in EORTC QLQ-C30 GHS |
| Comparison groups | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD v P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
| Number of subjects included in analysis | 532 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.2975 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.183 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.865 |
| upper limit | 1.619 |

Secondary: Randomized (Part 3): Change from baseline in Function Assessment Cancer Therapy-melanoma (FACT-M) melanoma subscale score

| | |
|-----------------|---|
| End point title | Randomized (Part 3): Change from baseline in Function Assessment Cancer Therapy-melanoma (FACT-M) melanoma subscale score ^[12] |
|-----------------|---|

End point description:

The Functional Assessment of Cancer Therapy-Melanoma (FACT-M) quality of life questionnaire was composed of the FACT-General (FACT-G) plus the Melanoma Subscale and the Melanoma Surgery

Subscale, which complemented the general scale with items specific to quality of life (QoL) in melanoma. The Melanoma Subscale of FACT-M included 16 questions, with response options of 0= "Not at all", 1= "a little bit", 2= "somewhat", 3= "quite a bit" and 4= "very much". The FACT-M melanoma subscale score ranged from 0 to 64, with higher scores indicating a higher quality of life in relation to melanoma. The change from baseline in melanoma subscale scores was calculated. A positive change from baseline indicated improvement.

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

End point timeframe:

From baseline to 60 days post progression, assessed up to 2.8 years (Part 3)

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 applicable to Part 3-Arm 1 and Part 3-Arm 2

| End point values | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 177 | 190 | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 4 Day 1 | 0.83 (± 6.600) | 0.87 (± 6.185) | | |
| Cycle 6 Day 1 | 1.01 (± 7.370) | 1.18 (± 6.219) | | |
| Cycle 8 Day 1 | 1.14 (± 7.284) | 1.09 (± 5.742) | | |
| Cycle 10 Day 1 | 1.52 (± 7.314) | 0.54 (± 6.492) | | |
| Cycle 12 Day 1 | 1.21 (± 7.515) | 0.47 (± 5.974) | | |
| Cycle 14 Day 1 | 0.77 (± 7.071) | 0.65 (± 6.681) | | |
| Cycle 16 Day 1 | 0.93 (± 6.451) | 0.71 (± 6.374) | | |
| Cycle 18 Day 1 | 1.23 (± 7.095) | 0.47 (± 6.152) | | |
| Cycle 20 Day 1 | 1.28 (± 6.634) | 0.53 (± 5.875) | | |
| Cycle 22 Day 1 | 1.87 (± 6.215) | 0.79 (± 5.970) | | |
| Cycle 25 Day 1 | 2.73 (± 5.950) | 0.74 (± 6.792) | | |
| Cycle 28 Day 1 | 2.46 (± 5.195) | 0.61 (± 8.020) | | |
| Cycle 31 Day 1 | 3.29 (± 5.702) | 1.88 (± 6.154) | | |
| Cycle 34 Day 1 | -0.50 (± 2.121) | 4.60 (± 3.578) | | |
| 30 days post-progression | 0.33 (± 7.620) | -1.07 (± 8.590) | | |
| 60 days post-progression | -2.60 (± 5.734) | -3.06 (± 8.948) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized (Part 3): Change from baseline in EuroQoL 5-level instrument (EQ-5D-5L)- Visual Analog Scale (VAS) score

| | |
|-----------------|---|
| End point title | Randomized (Part 3): Change from baseline in EuroQoL 5-level instrument (EQ-5D-5L)- Visual Analog Scale (VAS) score ^[13] |
|-----------------|---|

End point description:

The EQ-5D-5L is a standardized questionnaire used to assess health-related quality of life, and it

includes a Visual Analog Scale (VAS). The VAS score is obtained by asking the individual to rate their current health status on a scale from 0 to 100, where 0 represents the worst possible health state and 100 represents the best possible health state. The change from baseline in EQ-5D-5L VAS score was calculated. A positive change from baseline indicates improvement in the health status.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From baseline to 60 days post progression, assessed up to 2.8 years (Part 3) | |

Notes:

[13] - 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 applicable to Part 3-Arm 1 and Part 3-Arm 2

| End point values | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 176 | 190 | | |
| Units: Score on a Scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 4 Day 1 | 1.85 (± 16.567) | 2.16 (± 19.733) | | |
| Cycle 6 Day 1 | 1.55 (± 20.751) | 3.10 (± 16.095) | | |
| Cycle 8 Day 1 | 0.39 (± 20.246) | 2.60 (± 15.200) | | |
| Cycle 10 Day 1 | 2.45 (± 19.050) | 2.52 (± 16.144) | | |
| Cycle 12 Day 1 | 1.88 (± 24.653) | 1.42 (± 15.695) | | |
| Cycle 14 Day 1 | 2.62 (± 19.455) | 1.71 (± 14.337) | | |
| Cycle 16 Day 1 | 1.30 (± 18.640) | 2.79 (± 16.996) | | |
| Cycle 18 Day 1 | 2.16 (± 20.762) | 1.91 (± 16.743) | | |
| Cycle 20 Day 1 | 1.34 (± 17.831) | 1.28 (± 16.108) | | |
| Cycle 22 Day 1 | 3.01 (± 19.102) | 1.55 (± 14.973) | | |
| Cycle 25 Day 1 | 4.47 (± 19.489) | 0.26 (± 14.784) | | |
| Cycle 28 Day 1 | 4.20 (± 17.545) | -0.39 (± 18.529) | | |
| Cycle 31 Day 1 | 6.45 (± 19.561) | -0.08 (± 16.747) | | |
| Cycle 34 Day 1 | -9.50 (± 14.849) | 5.60 (± 19.008) | | |
| 30 days post-progression | -4.04 (± 22.033) | -10.24 (± 23.532) | | |
| 60 days post-progression | -19.25 (± 19.923) | -8.19 (± 21.192) | | |

Statistical analyses

Secondary: Randomized (Part 3): PFS as per investigator's assessment by RECIST 1.1 by PD-L1 expression

| | |
|-----------------|---|
| End point title | Randomized (Part 3): PFS as per investigator's assessment by RECIST 1.1 by PD-L1 expression ^[14] |
|-----------------|---|

End point description:

PFS was defined as the time from the date of first dose to the date of the first documented radiological progression as per investigator's assessment using RECIST 1.1 response criteria or death due to any cause. The distribution of PFS was estimated using the KM method. If a patient had not had an event at the time of data cut-off, progression-free survival was censored at the date of last adequate tumor assessment. PFS analysis was performed by PD-L1 status (positive, negative) where a positive status was defined as having $\geq 1\%$ expression and a negative status was defined as having $< 1\%$ expression.

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

End point timeframe:

Up to disease progression or death due to any cause, up to 2.8 years (Part 3)

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 applicable to Part 3-Arm 1 and Part 3-Arm 2

| End point values | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD | | |
|----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 236 | 241 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| PD-L1 negative ($<1\%$) | 12.0 (10.1 to 15.7) | 10.3 (7.5 to 13.0) | | |
| PD-L1 positive ($\geq 1\%$) | 26.6 (17.4 to 999) | 15.4 (10.2 to 25.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Randomized (Part 3): OS by PD-L1 expression

| | |
|-----------------|---|
| End point title | Randomized (Part 3): OS by PD-L1 expression ^[15] |
|-----------------|---|

End point description:

Overall survival was defined as the time from date of randomization to date of death due to any cause. OS analysis was performed by PD-L1 subgroup (positive, negative) where a positive status was defined as having $\geq 1\%$ expression and a negative status was defined as having $< 1\%$ expression.

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

End point timeframe:

Up to death due to any cause, assessed up to approximately 7 years

Notes:

[15] - 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 applicable to Part 3-Arm 1 and Part 3-Arm 2

| | | | | |
|----------------------------------|---|---|--|--|
| End point values | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 112 | 138 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| PD-L1 negative (<1%) | 41.6 (27.6 to 999) | 21.0 (16.9 to 33.4) | | |
| PD-L1 positive (>=1%) | 999 (45.4 to 999) | 61.3 (41.2 to 999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Spartalizumab Anti-drug Antibody (ADA) prevalence at baseline

| | |
|---|--|
| End point title | Spartalizumab Anti-drug Antibody (ADA) prevalence at |
| End point description: Spartalizumab ADA prevalence at baseline was calculated as the percentage of participants who had an spartalizumab ADA positive result at baseline. | |
| End point type | Secondary |
| End point timeframe: Baseline | |
| 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 applicable to Part 1, Part 2 and Part 3-Arm 1 | |

| | | | | |
|-----------------------------|---|--|---|--|
| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | |
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 9 | 26 | 244 | |
| Units: Participants | 0 | 0 | 4 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Spartalizumab ADA incidence

| | |
|---|---|
| End point title | Spartalizumab ADA incidence ^[17] |
| End point description: Spartalizumab ADA incidence was calculated as the percentage of participants who were treatment-induced spartalizumab ADA positive (post-baseline ADA positive with ADA-negative sample at baseline) and treatment-boosted spartalizumab ADA positive (post-baseline ADA positive with titer that is at least | |

the fold titer change greater than the ADA-positive baseline titer)

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Throughout study until 150 days after the last dose of spartalizumab, up to 3.3 years (Part 1), 3 years (Part 2) and 2.8 years (Part 3). | |

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 applicable to Part 1, Part 2 and Part 3-Arm 1

| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | |
|-----------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 9 | 26 | 244 | |
| Units: Participants | 0 | 5 | 55 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Trough concentration (C_{trough}) for spartalizumab

| | |
|---|---|
| End point title | Trough concentration (C _{trough}) for spartalizumab ^[18] |
| End point description: | |
| C _{trough} for spartalizumab refers to the serum concentration of spartalizumab immediately prior to the administration of a dose of spartalizumab on Day 1 of Cycle 2 and later cycles. | |

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Pre-infusion on Day 1 of each Cycle starting from Cycle 2, up to 3.3 years (Part 1), 3 years (Part 2) and 2.8 years (Part 3). Cycle=28 days | |

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 applicable to Part 1, Part 2 and Part 3-Arm 1

| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | |
|--------------------------------------|---|--|---|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 5 | 17 | 138 | |
| Units: microgram (µg)/miliLiter (mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 2 | 31.9 (± 4.59) | 31.5 (± 20.3) | 28.4 (± 13.4) | |
| Cycle 3 | 41.1 (± 7.07) | 56.1 (± 34.2) | 43.5 (± 19.1) | |
| Cycle 4 | 47.8 (± 999) | 46.9 (± 18.8) | 50.5 (± 24.2) | |
| Cycle 5 | 46.3 (± 999) | 56.7 (± 19.5) | 56.4 (± 24.5) | |
| Cycle 6 | 53.8 (± 16.9) | 60.9 (± 23.6) | 58.8 (± 26.5) | |
| Cycle 7 | 56.1 (± 12.1) | 62.2 (± 33.3) | 63.7 (± 29.6) | |

| | | | | |
|----------|---------------|---------------|---------------|--|
| Cycle 8 | 57.9 (± 12.7) | 65.8 (± 32.8) | 64.1 (± 29.9) | |
| Cycle 9 | 60.2 (± 30.9) | 69.5 (± 25.2) | 67.8 (± 33.5) | |
| Cycle 10 | 62.1 (± 22.5) | 68.4 (± 33.2) | 63.8 (± 28.4) | |
| Cycle 11 | 66.9 (± 15.8) | 63.2 (± 35.8) | 62.1 (± 27.9) | |
| Cycle 12 | 67.0 (± 16.5) | 61.6 (± 29.3) | 60.7 (± 27.2) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose plasma concentration for dabrafenib

| | |
|------------------------|--|
| End point title | Pre-dose plasma concentration for dabrafenib |
| End point description: | Plasma concentration of dabrafenib immediately prior to the administration of a dose of dabrafenib. |
| End point type | Secondary |
| End point timeframe: | Pre-infusion on Day 1 of every cycle from Cycle 2 to 12, and then every 6 cycles from Cycle 18 to 36, up to 3.3 years (Part 1), 3 years (Part 2) and 2.8 years (Part 3). Cycle=28 days |

| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
|--------------------------------------|---|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 4 | 18 | 127 | 162 |
| Units: nanogram (ng)/ miliLiter (mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 2 | 33.7 (± 27.4) | 149 (± 391) | 208 (± 473) | 234 (± 475) |
| Cycle 3 | 25.5 (± 10.4) | 183 (± 469) | 192 (± 607) | 135 (± 266) |
| Cycle 4 | 23.0 (± 15.8) | 372 (± 811) | 169 (± 404) | 167 (± 328) |
| Cycle 5 | 28.8 (± 30.6) | 152 (± 293) | 130 (± 317) | 152 (± 363) |
| Cycle 6 | 15.1 (± 16.3) | 73.7 (± 131) | 198 (± 521) | 94.6 (± 186) |
| Cycle 7 | 20.9 (± 13.9) | 40.0 (± 20.0) | 180 (± 510) | 121 (± 279) |
| Cycle 8 | 22.9 (± 16.8) | 28.0 (± 10.4) | 173 (± 532) | 97.2 (± 177) |
| Cycle 9 | 22.3 (± 7.59) | 43.3 (± 40.6) | 143 (± 394) | 133 (± 259) |
| Cycle 10 | 24.5 (± 9.19) | 60.0 (± 28.3) | 167 (± 472) | 122 (± 266) |
| Cycle 11 | 154 (± 250) | 33.8 (± 22.6) | 174 (± 667) | 119 (± 238) |
| Cycle 12 | 10.9 (± 10.3) | 41.3 (± 37.2) | 148 (± 396) | 146 (± 295) |
| Cycle 18 | 19.0 (± 999) | 50.6 (± 49.7) | 180 (± 618) | 167 (± 385) |
| Cycle 24 | 999 (± 999) | 91.5 (± 98.3) | 147 (± 344) | 60.2 (± 67.9) |
| Cycle 30 | 40.2 (± 999) | 999 (± 999) | 226 (± 488) | 47.6 (± 23.2) |
| Cycle 36 | 47.6 (± 999) | 999 (± 999) | 999 (± 999) | 999 (± 999) |

Statistical analyses

Secondary: Pre-dose plasma concentration for trametinib

| | |
|--|--|
| End point title | Pre-dose plasma concentration for trametinib |
| End point description: Plasma concentration of trametinib immediately prior to the administration of a dose of trametinib. | |
| End point type | Secondary |
| End point timeframe: Pre-infusion on Day 1 of every cycle from Cycle 2 to 12, and then every 6 cycles from Cycle 18 to 36, up to 3.3 years (Part 1), 3 years (Part 2) and 2.8 years (Part 3). Cycle=28 days | |

| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
|--------------------------------------|---|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 14 | 103 | 143 |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 2 | 11.7 (± 4.09) | 11.2 (± 3.4) | 11.5 (± 4.73) | 13.9 (± 9.36) |
| Cycle 3 | 8.34 (± 0.354) | 12.2 (± 2.55) | 11.4 (± 5.98) | 12.3 (± 5.59) |
| Cycle 4 | 10.7 (± 1.64) | 12.5 (± 4.84) | 11.7 (± 4.62) | 11.9 (± 5.04) |
| Cycle 5 | 10.1 (± 999) | 12.6 (± 5.03) | 11.3 (± 4.91) | 11.6 (± 4.49) |
| Cycle 6 | 10.0 (± 1.38) | 11.8 (± 3.73) | 11.6 (± 5.12) | 10.9 (± 3.52) |
| Cycle 7 | 11.6 (± 3.8) | 11.8 (± 5.24) | 12.0 (± 4.86) | 11.0 (± 4.26) |
| Cycle 8 | 9.24 (± 3.06) | 10.2 (± 4.13) | 10.3 (± 3.92) | 11.3 (± 4.08) |
| Cycle 9 | 8.73 (± 3.35) | 10.5 (± 4.43) | 10.9 (± 4.57) | 11.6 (± 4.22) |
| Cycle 10 | 8.24 (± 999) | 10.5 (± 4.02) | 10.9 (± 4.47) | 11.8 (± 4.26) |
| Cycle 11 | 10.7 (± 999) | 11.6 (± 4.69) | 10.3 (± 3.67) | 11.4 (± 3.57) |
| Cycle 12 | 10.6 (± 3.92) | 11.0 (± 4.53) | 10.6 (± 4.31) | 11.2 (± 3.82) |
| Cycle 18 | 10.1 (± 999) | 13.0 (± 4.6) | 9.66 (± 3.49) | 12.1 (± 5.13) |
| Cycle 24 | 999 (± 999) | 13.4 (± 8.03) | 10.7 (± 4.89) | 10.7 (± 2.21) |
| Cycle 30 | 10.8 (± 999) | 999 (± 999) | 9.34 (± 7.56) | 10.1 (± 2.76) |
| Cycle 36 | 8.97 (± 999) | 999 (± 999) | 999 (± 999) | 999 (± 999) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with dose interruptions

| | |
|---|--|
| End point title | Number of participants with dose interruptions |
| End point description: Number of participants with dose interruptions for spartalizumab, dabrafenib and trametinib | |
| End point type | Secondary |
| End point timeframe: From baseline to end of treatment, assessed up to approximately 7 years | |

| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
|---|---|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 27 | 267 | 264 |
| Units: Participants | | | | |
| Spartalizumab With no dose interruption | 4 | 11 | 120 | 170 |
| Dabrafenib With no dose interruption | 0 | 2 | 29 | 74 |
| Trametinib With no dose interruption | 0 | 1 | 29 | 64 |
| Spartalizumab With at least one dose interruption | 5 | 16 | 147 | 94 |
| Dabrafenib With at least one dose interruption | 9 | 25 | 238 | 190 |
| Trametinib With at least one dose interruption | 9 | 26 | 238 | 200 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with dose reductions

| | |
|--|---|
| End point title | Number of participants with dose reductions |
| End point description: | |
| Number of patients with dose reductions for spartalizumab, dabrafenib and trametinib | |
| End point type | Secondary |
| End point timeframe: | |
| From baseline to end of treatment, assessed up to approximately 7 years | |

| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
|--|---|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 27 | 267 | 264 |
| Units: Participants | | | | |
| Dabrafenib No dose reduction or interruption | 0 | 2 | 25 | 68 |
| Trametinib No dose reduction or interruption | 0 | 1 | 28 | 63 |
| Dabrafenib ≥1 dose red./interruption | 9 | 25 | 242 | 196 |
| Trametinib ≥1 dose red./interruption | 9 | 26 | 239 | 201 |

Statistical analyses

No statistical analyses for this end point

Secondary: Relative dose intensity

| | |
|-----------------|-------------------------|
| End point title | Relative dose intensity |
|-----------------|-------------------------|

End point description:

Relative dose intensity for spartalizumab, dabrafenib and trametinib computed as the ratio (expressed as percentage) of dose intensity and planned dose intensity:

* Spartalizumab (PDR001) = [Dose intensity (mg/4W) / planned dose intensity (mg/4W)]*100.

* Trametinib and Dabrafenib = [Dose intensity (mg/day) / planned dose intensity (mg/day)]*100.

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

End point timeframe:

From baseline to end of treatment, assessed up to approximately 7 years

| End point values | P1-Safety: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P2-Biomarker: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm1: PDR001 400mg Q4W + dab 150mg BID + tram 2mg QD | P3-Arm2: Placebo + dab 150mg BID + tram 2mg QD |
|---|---|--|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 27 | 267 | 264 |
| Units: Percentage of planned dose intensity | | | | |
| arithmetic mean (standard deviation) | | | | |
| Spartalizumab (PDR001) | 90.7 (± 16.83) | 91.7 (± 10.41) | 94.4 (± 9.21) | 97.5 (± 5.33) |
| Dabrafenib | 62.2 (± 26.36) | 71.3 (± 21.13) | 78.1 (± 21.21) | 89.6 (± 15.10) |
| Trametinib | 65.9 (± 16.90) | 76.2 (± 17.19) | 79.8 (± 19.58) | 89.5 (± 14.86) |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected from first dose of study medication until the last dose plus 30 days safety follow-up, assessed up to approximately 86 months.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

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

Dictionary used

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

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

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | Part I PDR001 + D + T |
|-----------------------|-----------------------|

Reporting group description:

Part I PDR001 + D + T

| | |
|-----------------------|--------------------------|
| Reporting group title | Part III Placebo + D + T |
|-----------------------|--------------------------|

Reporting group description:

Part III Placebo + D + T

| | |
|-----------------------|-------------------------|
| Reporting group title | Part III PDR001 + D + T |
|-----------------------|-------------------------|

Reporting group description:

Part III PDR001 + D + T

| | |
|-----------------------|------------------------|
| Reporting group title | Part II PDR001 + D + T |
|-----------------------|------------------------|

Reporting group description:

Part II PDR001 + D + T

| Serious adverse events | Part I PDR001 + D + T | Part III Placebo + D + T | Part III PDR001 + D + T |
|---|-----------------------|--------------------------|-------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 9 (77.78%) | 123 / 264 (46.59%) | 151 / 267 (56.55%) |
| number of deaths (all causes) | 2 | 33 | 28 |
| number of deaths resulting from adverse events | 0 | 2 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to meninges | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |

| | | | |
|---|---------------|-----------------|-----------------|
| Malignant melanoma in situ | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Benign breast neoplasm | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 264 (1.14%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 8 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenocarcinoma pancreas | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neoplasm malignant | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-Hodgkin's lymphoma | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oncologic complication | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Squamous cell carcinoma | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyroid neoplasm | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 neoplasm | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Uterine neoplasm | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Vascular disorders | | | |
| Aneurysm ruptured | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Embolism | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematoma | | | |

| | | | |
|--|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Vasculitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Lymphoedema | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shock haemorrhagic | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Administration site extravasation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Generalised oedema | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 4 / 267 (1.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chills | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 3 / 267 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Discomfort | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 3 / 267 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 3 / 267 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Multiple organ dysfunction syndrome | | | |

| | | | |
|---|----------------|------------------|-------------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 9 (44.44%) | 16 / 264 (6.06%) | 46 / 267 (17.23%) |
| occurrences causally related to treatment / all | 7 / 7 | 22 / 25 | 65 / 70 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Contrast media allergy | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Sarcoidosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemophagocytic lymphohistiocytosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Reproductive system and breast disorders | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| Benign prostatic hyperplasia subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Prostatic disorder subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 | | | |
| Autoimmune lung disease subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cough subjects affected / exposed | 0 / 9 (0.00%) | 3 / 264 (1.14%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Interstitial lung disease subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung disorder subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|-----------------|
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 6 / 264 (2.27%) | 7 / 267 (2.62%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 6 | 2 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 9 / 267 (3.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 9 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Respiratory arrest | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anxiety | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alanine aminotransferase abnormal | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase abnormal | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|------------------|------------------|
| Amylase increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 4 / 267 (1.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Body temperature increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General physical condition abnormal | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 15 / 264 (5.68%) | 17 / 267 (6.37%) |
| occurrences causally related to treatment / all | 1 / 1 | 16 / 18 | 18 / 18 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lipase increased | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Streptococcus test positive | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Craniocerebral injury | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Fall | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Head injury | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infusion related reaction | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post embolisation syndrome | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Scapula fracture | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Subdural haematoma | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound haemorrhage | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arteriosclerosis coronary artery | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| 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 disorder | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 3 / 267 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery stenosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinus node dysfunction | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 | | | |
| Altered state of consciousness | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Amnesia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aphasia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Brain oedema | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 264 (1.14%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| Cerebral haematoma | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 3 / 267 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| Epilepsy | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 0 / 267 (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 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cognitive disorder | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 264 (1.14%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 4 / 264 (1.52%) | 3 / 267 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 4 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningism | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic cerebral infarction | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Intracranial tumour haemorrhage | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intracranial pressure increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Immune-mediated encephalopathy | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydrocephalus | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Monoparesis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Nerve compression | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorder | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Neuritis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neurological decompensation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Partial seizures | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Peripheral motor neuropathy | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Polyneuropathy | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 264 (1.14%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Presyncope | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sciatica | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 / 9 (0.00%) | 4 / 264 (1.52%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Febrile neutropenia | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Lymphadenopathy mediastinal | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Eye disorders | | | |
| Conjunctival haemorrhage | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Cataract | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angle closure glaucoma | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Detachment of retinal pigment | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| epithelium | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diplopia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uveitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 3 / 267 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal detachment | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal degeneration | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Macular detachment | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Iridocyclitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 5 / 267 (1.87%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 5 / 267 (1.87%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 5 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune colitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Abdominal wall haematoma | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis ischaemic | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Colitis ulcerative | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Constipation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 3 / 267 (1.12%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Intestinal perforation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Umbilical hernia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 5 / 264 (1.89%) | 3 / 267 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 5 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 | | | |
| Autoimmune hepatitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 4 / 267 (1.50%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholelithiasis | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic failure | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Hepatitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Portal vein thrombosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver disorder | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune-mediated hepatitis | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatitis exfoliative generalised | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| 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 | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxic skin eruption | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Immune-mediated nephritis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematuria | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Calculus urinary | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 9 / 267 (3.37%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 3 | 6 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephritis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urethral stenosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Tubulointerstitial nephritis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal colic | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 0 / 267 (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 |
| Urinary retention | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Hypophysitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 / 9 (0.00%) | 2 / 264 (0.76%) | 3 / 267 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |

| | | | |
|---|---------------|-----------------|-----------------|
| Back pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 4 / 264 (1.52%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle haemorrhage | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Soft tissue necrosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sacral pain | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Pathological fracture | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis perforated | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial food poisoning | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacterial sepsis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Biliary tract infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 5 / 267 (1.87%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Empyema | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Meningitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash pustular | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 264 (1.14%) | 5 / 267 (1.87%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 1 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Post procedural sepsis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 3 / 267 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic infection | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sweating fever | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 2 / 267 (0.75%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 264 (1.14%) | 5 / 267 (1.87%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 1 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Urinary tract infection fungal | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 3 / 267 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |

| | | | |
|---|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 0 / 267 (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 |
| Hypomagnesaemia | | | |

| | | | |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (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 |

| Serious adverse events | Part II PDR001 + D + T | | |
|---|------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 18 / 27 (66.67%) | | |
| number of deaths (all causes) | 3 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenocarcinoma of colon | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metastases to meninges | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant melanoma in situ | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant melanoma | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Benign breast neoplasm | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Basal cell carcinoma | | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Adenocarcinoma pancreas | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neoplasm malignant | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Non-Hodgkin's lymphoma | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oncologic complication | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Squamous cell carcinoma | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Squamous cell carcinoma of skin | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thyroid neoplasm | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary tract neoplasm | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Uterine neoplasm | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Aneurysm ruptured | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Embolism | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haematoma | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vasculitis | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphoedema | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Shock haemorrhagic | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Administration site extravasation | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chills | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Discomfort | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fatigue | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General physical health deterioration | | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oedema peripheral | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Multiple organ dysfunction syndrome | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Malaise | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pain | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyrexia | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 4 / 27 (14.81%) | | |
| occurrences causally related to treatment / all | 8 / 8 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Contrast media allergy | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sarcoidosis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemophagocytic lymphohistiocytosis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Prostatic disorder | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Autoimmune lung disease | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cough | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dyspnoea | | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Epistaxis | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Interstitial lung disease | | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung disorder | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary embolism | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumothorax | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonitis | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory arrest | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Confusional state | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |

| | | | | |
|---|----------------|--|--|--|
| Alanine aminotransferase increased | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Alanine aminotransferase abnormal | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood creatine phosphokinase increased | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood bilirubin increased | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aspartate aminotransferase increased | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aspartate aminotransferase abnormal | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Amylase increased | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood creatinine increased | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | | |
|--|-----------------|--|--|--|
| Body temperature increased subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatic enzyme increased subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General physical condition abnormal subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Electrocardiogram QT prolonged subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ejection fraction decreased subjects affected / exposed | 3 / 27 (11.11%) | | | |
| occurrences causally related to treatment / all | 3 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| C-reactive protein increased subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lipase increased subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Streptococcus test positive subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Transaminases increased | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Craniocerebral injury | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fall | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Head injury | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower limb fracture | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Overdose | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post embolisation syndrome | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Scapula fracture | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Road traffic accident | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound haemorrhage | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial flutter | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arteriosclerosis coronary artery | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Angina unstable | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bradycardia | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac arrest | | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Cardiac disorder | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Left ventricular dysfunction | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Coronary artery stenosis | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinus node dysfunction | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Altered state of consciousness | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Amnesia | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aphasia | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Brain oedema | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cerebral haematoma | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cerebral haemorrhage | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Epilepsy | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dysarthria | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dizziness | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cognitive disorder | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cerebral infarction | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cerebrovascular accident | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Headache | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meningism | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ischaemic cerebral infarction | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intracranial tumour haemorrhage | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intracranial pressure increased | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Immune-mediated encephalopathy | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hydrocephalus | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metabolic encephalopathy | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Monoparesis | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nerve compression | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nervous system disorder | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neuritis | | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neurological decompensation | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neuropathy peripheral | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Paraesthesia | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Partial seizures | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral motor neuropathy | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Polyneuropathy | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Presyncope | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sciatica | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Seizure | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal cord compression | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tremor | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphadenopathy | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphadenopathy mediastinal | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Conjunctival haemorrhage | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Angle closure glaucoma | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Detachment of retinal pigment epithelium | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diplopia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Vision blurred | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Uveitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Retinal detachment | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Retinal degeneration | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Macular detachment | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Iridocyclitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Autoimmune colitis | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ascites | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aphthous ulcer | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal wall haematoma | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal pain upper | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colitis ischaemic | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colitis ulcerative | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Constipation | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enteritis | | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Inguinal hernia | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal perforation | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower gastrointestinal haemorrhage | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nausea | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatitis | | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatitis acute | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rectal haemorrhage | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Umbilical hernia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Autoimmune hepatitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic failure | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertransaminaemia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Portal vein thrombosis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Liver disorder | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dermatitis acneiform | | | |

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|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dermatitis exfoliative generalised | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rash | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Toxic skin eruption | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Immune-mediated nephritis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Calculus urinary | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nephritis | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nephrolithiasis | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urethral stenosis | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tubulointerstitial nephritis | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal impairment | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal failure | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal colic | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary retention | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary tract obstruction | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| Hypophysitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bursitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|---|----------------|--|--|--|
| Intervertebral disc disorder | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intervertebral disc protrusion | | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Muscle haemorrhage | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Muscular weakness | | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spinal pain | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Soft tissue necrosis | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sacral pain | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rhabdomyolysis | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pathological fracture | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neck pain | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis perforated | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bacterial food poisoning | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bacterial sepsis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Biliary tract infection | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| COVID-19 | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| COVID-19 pneumonia | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterocolitis infectious | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Emphyema | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Device related infection | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Erysipelas | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumocystis jirovecii pneumonia | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Febrile infection | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infection | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Influenza | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract infection | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Meningitis | | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritonitis | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory tract infection | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rash pustular | | | | |

| | | | | |
|---|----------------|--|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyelonephritis | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post procedural infection | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post procedural sepsis | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary tract infection | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Systemic infection | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sweating fever | | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin infection | | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection fungal | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Wound infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetic ketoacidosis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gout | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Part I PDR001 + D + T | Part III Placebo + D + T | Part III PDR001 + D + T |
|---|--------------------------|-----------------------------|----------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 9 / 9 (100.00%) | 250 / 264 (94.70%) | 262 / 267 (98.13%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Fibrous histiocytoma | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 9 / 264 (3.41%) | 2 / 267 (0.75%) |
| occurrences (all) | 4 | 12 | 4 |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 4 / 264 (1.52%) | 5 / 267 (1.87%) |
| occurrences (all) | 0 | 5 | 5 |
| Superficial vein thrombosis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypotension | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 7 / 264 (2.65%) | 10 / 267 (3.75%) |
| occurrences (all) | 3 | 8 | 11 |
| Lymphoedema | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 4 / 264 (1.52%) | 7 / 267 (2.62%) |
| occurrences (all) | 1 | 4 | 7 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 264 (1.14%) | 0 / 267 (0.00%) |
| occurrences (all) | 0 | 4 | 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 34 / 264 (12.88%) | 20 / 267 (7.49%) |
| occurrences (all) | 0 | 43 | 25 |
| General disorders and administration site conditions | | | |
| Face oedema | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 8 / 267 (3.00%) |
| occurrences (all) | 1 | 2 | 9 |

| | | | |
|-------------------------------|-----------------|--------------------|--------------------|
| Fatigue | | | |
| subjects affected / exposed | 7 / 9 (77.78%) | 69 / 264 (26.14%) | 71 / 267 (26.59%) |
| occurrences (all) | 9 | 141 | 115 |
| Influenza like illness | | | |
| subjects affected / exposed | 4 / 9 (44.44%) | 15 / 264 (5.68%) | 28 / 267 (10.49%) |
| occurrences (all) | 6 | 21 | 208 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 1 / 264 (0.38%) | 5 / 267 (1.87%) |
| occurrences (all) | 2 | 1 | 5 |
| Oedema | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 7 / 264 (2.65%) | 3 / 267 (1.12%) |
| occurrences (all) | 0 | 7 | 3 |
| Oedema due to cardiac disease | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 8 / 9 (88.89%) | 63 / 264 (23.86%) | 86 / 267 (32.21%) |
| occurrences (all) | 17 | 148 | 303 |
| Axillary pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 264 (1.14%) | 4 / 267 (1.50%) |
| occurrences (all) | 0 | 3 | 4 |
| Asthenia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 55 / 264 (20.83%) | 73 / 267 (27.34%) |
| occurrences (all) | 2 | 116 | 107 |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 28 / 264 (10.61%) | 30 / 267 (11.24%) |
| occurrences (all) | 1 | 29 | 34 |
| Pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 10 / 264 (3.79%) | 7 / 267 (2.62%) |
| occurrences (all) | 1 | 14 | 10 |
| Pyrexia | | | |
| subjects affected / exposed | 9 / 9 (100.00%) | 145 / 264 (54.92%) | 189 / 267 (70.79%) |
| occurrences (all) | 59 | 670 | 1330 |
| Xerosis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 2 / 264 (0.76%) | 3 / 267 (1.12%) |
| occurrences (all) | 0 | 2 | 4 |

| | | | |
|---|----------------|-------------------|-------------------|
| Immune system disorders | | | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sarcoidosis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 5 / 267 (1.87%) |
| occurrences (all) | 1 | 2 | 5 |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 30 / 264 (11.36%) | 37 / 267 (13.86%) |
| occurrences (all) | 1 | 36 | 40 |
| Cough | | | |
| subjects affected / exposed | 6 / 9 (66.67%) | 49 / 264 (18.56%) | 63 / 267 (23.60%) |
| occurrences (all) | 10 | 63 | 102 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 8 / 264 (3.03%) | 17 / 267 (6.37%) |
| occurrences (all) | 2 | 9 | 31 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 11 / 264 (4.17%) | 10 / 267 (3.75%) |
| occurrences (all) | 4 | 12 | 11 |
| Pleurisy | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 4 / 264 (1.52%) | 28 / 267 (10.49%) |
| occurrences (all) | 3 | 4 | 38 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 6 / 264 (2.27%) | 12 / 267 (4.49%) |
| occurrences (all) | 1 | 6 | 12 |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|----------------------|-------------------------|--------------------------|
| Rhinorrhoea subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 5 / 264 (1.89%) 5 | 10 / 267 (3.75%) 13 |
| Sinus congestion subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 264 (0.00%) 0 | 1 / 267 (0.37%) 2 |
| Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 16 / 264 (6.06%) 18 | 12 / 267 (4.49%) 12 |
| Insomnia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 2 | 18 / 264 (6.82%) 22 | 22 / 267 (8.24%) 23 |
| Disorientation subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 264 (0.00%) 0 | 1 / 267 (0.37%) 1 |
| Bradyphrenia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 264 (0.00%) 0 | 0 / 267 (0.00%) 0 |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 3 / 9 (33.33%) 7 | 41 / 264 (15.53%) 69 | 67 / 267 (25.09%) 99 |
| Blood testosterone decreased subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 264 (0.00%) 0 | 0 / 267 (0.00%) 0 |
| Amylase increased subjects affected / exposed occurrences (all) | 4 / 9 (44.44%) 14 | 22 / 264 (8.33%) 30 | 46 / 267 (17.23%) 73 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 7 | 53 / 264 (20.08%) 77 | 76 / 267 (28.46%) 114 |
| Blood albumin decreased subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 264 (0.38%) 1 | 4 / 267 (1.50%) 4 |
| Blood alkaline phosphatase increased | | | |

| | | | |
|---|----------------|-------------------|-------------------|
| subjects affected / exposed | 2 / 9 (22.22%) | 28 / 264 (10.61%) | 33 / 267 (12.36%) |
| occurrences (all) | 6 | 38 | 63 |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 11 / 264 (4.17%) | 12 / 267 (4.49%) |
| occurrences (all) | 2 | 23 | 29 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 72 / 264 (27.27%) | 75 / 267 (28.09%) |
| occurrences (all) | 3 | 160 | 172 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 9 / 264 (3.41%) | 24 / 267 (8.99%) |
| occurrences (all) | 3 | 12 | 45 |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 21 / 264 (7.95%) | 27 / 267 (10.11%) |
| occurrences (all) | 4 | 41 | 44 |
| Blood sodium decreased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 1 / 267 (0.37%) |
| occurrences (all) | 1 | 3 | 1 |
| Blood thyroid stimulating hormone decreased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 5 / 267 (1.87%) |
| occurrences (all) | 1 | 2 | 5 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 3 / 267 (1.12%) |
| occurrences (all) | 1 | 4 | 6 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 11 / 264 (4.17%) | 12 / 267 (4.49%) |
| occurrences (all) | 3 | 13 | 12 |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 21 / 264 (7.95%) | 18 / 267 (6.74%) |
| occurrences (all) | 1 | 26 | 22 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 20 / 264 (7.58%) | 17 / 267 (6.37%) |
| occurrences (all) | 5 | 25 | 22 |
| Globulins increased | | | |

| | | | |
|--|----------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 5 / 264 (1.89%) | 5 / 267 (1.87%) |
| occurrences (all) | 0 | 5 | 6 |
| Lipase increased | | | |
| subjects affected / exposed | 5 / 9 (55.56%) | 38 / 264 (14.39%) | 66 / 267 (24.72%) |
| occurrences (all) | 11 | 65 | 131 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 5 / 264 (1.89%) | 5 / 267 (1.87%) |
| occurrences (all) | 0 | 6 | 7 |
| Myoglobin blood increased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences (all) | 1 | 0 | 3 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 11 / 264 (4.17%) | 8 / 267 (3.00%) |
| occurrences (all) | 3 | 12 | 16 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 6 / 264 (2.27%) | 9 / 267 (3.37%) |
| occurrences (all) | 0 | 6 | 13 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 11 / 264 (4.17%) | 17 / 267 (6.37%) |
| occurrences (all) | 0 | 12 | 25 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 6 / 264 (2.27%) | 9 / 267 (3.37%) |
| occurrences (all) | 1 | 6 | 12 |
| Injury, poisoning and procedural complications | | | |
| Compression fracture | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Contusion | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 2 / 267 (0.75%) |
| occurrences (all) | 1 | 2 | 2 |
| Procedural pain | | | |

| | | | |
|-----------------------------|----------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences (all) | 1 | 0 | 3 |
| Radiation skin injury | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nervous system disorders | | | |
| Anosmia | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Aphasia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 4 / 267 (1.50%) |
| occurrences (all) | 1 | 2 | 4 |
| Dizziness | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 23 / 264 (8.71%) | 21 / 267 (7.87%) |
| occurrences (all) | 2 | 30 | 25 |
| Syncope | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 3 / 264 (1.14%) | 2 / 267 (0.75%) |
| occurrences (all) | 0 | 4 | 2 |
| Peroneal nerve palsy | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 14 / 264 (5.30%) | 14 / 267 (5.24%) |
| occurrences (all) | 0 | 18 | 17 |
| Migraine | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 2 / 267 (0.75%) |
| occurrences (all) | 1 | 2 | 6 |
| Memory impairment | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 1 / 267 (0.37%) |
| occurrences (all) | 1 | 2 | 1 |
| Headache | | | |
| subjects affected / exposed | 5 / 9 (55.56%) | 74 / 264 (28.03%) | 80 / 267 (29.96%) |
| occurrences (all) | 31 | 188 | 208 |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 6 / 264 (2.27%) | 13 / 267 (4.87%) |
| occurrences (all) | 0 | 6 | 14 |

| | | | |
|--|---------------------|-------------------------|--------------------------|
| Dysaesthesia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 2 / 264 (0.76%) 2 | 2 / 267 (0.75%) 2 |
| Dizziness postural subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 264 (0.00%) 0 | 0 / 267 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Leukopenia subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 3 | 14 / 264 (5.30%) 21 | 23 / 267 (8.61%) 50 |
| Anaemia subjects affected / exposed occurrences (all) | 4 / 9 (44.44%) 6 | 31 / 264 (11.74%) 70 | 49 / 267 (18.35%) 92 |
| Lymphopenia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 3 | 11 / 264 (4.17%) 12 | 20 / 267 (7.49%) 30 |
| Thrombocytosis subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 264 (0.38%) 2 | 3 / 267 (1.12%) 3 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 2 | 10 / 264 (3.79%) 23 | 24 / 267 (8.99%) 43 |
| Neutropenia subjects affected / exposed occurrences (all) | 4 / 9 (44.44%) 8 | 37 / 264 (14.02%) 75 | 44 / 267 (16.48%) 111 |
| Ear and labyrinth disorders | | | |
| Ear congestion subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 264 (0.00%) 0 | 1 / 267 (0.37%) 1 |
| Ear pain subjects affected / exposed occurrences (all) | 3 / 9 (33.33%) 5 | 1 / 264 (0.38%) 1 | 1 / 267 (0.37%) 1 |
| Motion sickness subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 264 (0.00%) 0 | 0 / 267 (0.00%) 0 |
| Eye disorders | | | |

| | | | |
|-----------------------------|----------------|------------------|------------------|
| Dry eye | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 9 / 264 (3.41%) | 5 / 267 (1.87%) |
| occurrences (all) | 0 | 13 | 6 |
| Myopia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Iridocyclitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 264 (1.14%) | 3 / 267 (1.12%) |
| occurrences (all) | 1 | 4 | 3 |
| Ocular discomfort | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences (all) | 0 | 0 | 1 |
| Papilloedema | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 2 / 267 (0.75%) |
| occurrences (all) | 1 | 1 | 2 |
| Vitreous cells | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 6 / 264 (2.27%) | 10 / 267 (3.75%) |
| occurrences (all) | 0 | 7 | 10 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 13 / 264 (4.92%) | 9 / 267 (3.37%) |
| occurrences (all) | 0 | 16 | 10 |
| Uveitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 4 / 264 (1.52%) | 7 / 267 (2.62%) |
| occurrences (all) | 3 | 5 | 8 |
| Retinopathy | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Retinal haemorrhage | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences (all) | 1 | 0 | 1 |
| Photophobia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 264 (1.14%) | 6 / 267 (2.25%) |
| occurrences (all) | 1 | 3 | 6 |

| | | | |
|--|---------------------|--------------------------|--------------------------|
| Periorbital oedema subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 264 (0.38%) 1 | 4 / 267 (1.50%) 4 |
| Gastrointestinal disorders | | | |
| Abdominal distension subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 5 / 264 (1.89%) 6 | 2 / 267 (0.75%) 2 |
| Glossitis subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 264 (0.38%) 1 | 0 / 267 (0.00%) 0 |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 6 / 264 (2.27%) 25 | 9 / 267 (3.37%) 10 |
| Dyspepsia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 13 / 264 (4.92%) 17 | 18 / 267 (6.74%) 21 |
| Dry mouth subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 13 / 264 (4.92%) 14 | 22 / 267 (8.24%) 26 |
| Nausea subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 4 | 78 / 264 (29.55%) 136 | 90 / 267 (33.71%) 162 |
| Constipation subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 2 | 40 / 264 (15.15%) 49 | 40 / 267 (14.98%) 55 |
| Cheilitis subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 264 (0.00%) 0 | 0 / 267 (0.00%) 0 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 2 | 17 / 264 (6.44%) 29 | 26 / 267 (9.74%) 39 |
| Abdominal pain subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 26 / 264 (9.85%) 40 | 29 / 267 (10.86%) 42 |
| Diarrhoea | | | |

| | | | |
|--|----------------|-------------------|-------------------|
| subjects affected / exposed | 4 / 9 (44.44%) | 70 / 264 (26.52%) | 98 / 267 (36.70%) |
| occurrences (all) | 7 | 173 | 182 |
| Vomiting | | | |
| subjects affected / exposed | 4 / 9 (44.44%) | 50 / 264 (18.94%) | 69 / 267 (25.84%) |
| occurrences (all) | 11 | 116 | 128 |
| Odynophagia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 4 / 264 (1.52%) | 4 / 267 (1.50%) |
| occurrences (all) | 1 | 10 | 4 |
| Trichoglossia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Hepatic cytolysis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 7 / 264 (2.65%) | 5 / 267 (1.87%) |
| occurrences (all) | 0 | 10 | 5 |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hepatic steatosis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 4 / 264 (1.52%) | 6 / 267 (2.25%) |
| occurrences (all) | 3 | 6 | 7 |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 1 / 267 (0.37%) |
| occurrences (all) | 1 | 0 | 1 |
| Hepatitis | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 3 / 264 (1.14%) | 5 / 267 (1.87%) |
| occurrences (all) | 2 | 5 | 6 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 14 / 264 (5.30%) | 13 / 267 (4.87%) |
| occurrences (all) | 5 | 16 | 14 |
| Dry skin | | | |

| | | | |
|-----------------------------|----------------|------------------|-------------------|
| subjects affected / exposed | 0 / 9 (0.00%) | 15 / 264 (5.68%) | 14 / 267 (5.24%) |
| occurrences (all) | 0 | 15 | 17 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 9 / 264 (3.41%) | 17 / 267 (6.37%) |
| occurrences (all) | 0 | 9 | 17 |
| Eczema | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 16 / 264 (6.06%) | 9 / 267 (3.37%) |
| occurrences (all) | 1 | 19 | 10 |
| Erythema | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 11 / 264 (4.17%) | 27 / 267 (10.11%) |
| occurrences (all) | 0 | 12 | 37 |
| Photosensitivity reaction | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 264 (1.14%) | 9 / 267 (3.37%) |
| occurrences (all) | 1 | 3 | 12 |
| Panniculitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 8 / 264 (3.03%) | 9 / 267 (3.37%) |
| occurrences (all) | 3 | 12 | 15 |
| Palmoplantar keratoderma | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 11 / 264 (4.17%) | 10 / 267 (3.75%) |
| occurrences (all) | 4 | 18 | 26 |
| Ingrowing nail | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 3 / 267 (1.12%) |
| occurrences (all) | 1 | 1 | 3 |
| Hyperkeratosis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 5 / 267 (1.87%) |
| occurrences (all) | 1 | 1 | 7 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 14 / 264 (5.30%) | 7 / 267 (2.62%) |
| occurrences (all) | 12 | 15 | 7 |
| Granuloma annulare | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Erythema nodosum | | | |

| | | | |
|-----------------------------|----------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 9 (11.11%) | 9 / 264 (3.41%) | 14 / 267 (5.24%) |
| occurrences (all) | 6 | 12 | 14 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 22 / 264 (8.33%) | 51 / 267 (19.10%) |
| occurrences (all) | 3 | 26 | 89 |
| Skin disorder | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Sensitive skin | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Seborrhoeic dermatitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 4 / 264 (1.52%) | 1 / 267 (0.37%) |
| occurrences (all) | 1 | 4 | 2 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 7 / 267 (2.62%) |
| occurrences (all) | 0 | 1 | 8 |
| Stasis dermatitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences (all) | 1 | 1 | 3 |
| Rash macular | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 3 / 264 (1.14%) | 2 / 267 (0.75%) |
| occurrences (all) | 2 | 4 | 2 |
| Rash erythematous | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 5 / 267 (1.87%) |
| occurrences (all) | 1 | 1 | 5 |
| Rash | | | |
| subjects affected / exposed | 4 / 9 (44.44%) | 68 / 264 (25.76%) | 76 / 267 (28.46%) |
| occurrences (all) | 11 | 97 | 115 |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences (all) | 0 | 1 | 1 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 6 / 264 (2.27%) | 16 / 267 (5.99%) |
| occurrences (all) | 2 | 39 | 21 |
| Urticaria | | | |

| | | | |
|---|---------------------|------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 3 | 7 / 264 (2.65%) 7 | 6 / 267 (2.25%) 6 |
| Vitiligo subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 3 / 264 (1.14%) 3 | 21 / 267 (7.87%) 21 |
| Renal and urinary disorders | | | |
| Dysuria subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 8 / 264 (3.03%) 11 | 14 / 267 (5.24%) 19 |
| Haematuria subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 9 / 264 (3.41%) 9 | 8 / 267 (3.00%) 8 |
| Nocturia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 1 / 264 (0.38%) 1 | 0 / 267 (0.00%) 0 |
| Acute kidney injury subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 1 / 264 (0.38%) 1 | 6 / 267 (2.25%) 8 |
| Endocrine disorders | | | |
| Hypophysitis subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 264 (0.00%) 0 | 1 / 267 (0.37%) 1 |
| Hyperthyroidism subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 2 | 5 / 264 (1.89%) 5 | 18 / 267 (6.74%) 22 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 4 / 9 (44.44%) 4 | 17 / 264 (6.44%) 19 | 20 / 267 (7.49%) 24 |
| Inappropriate antidiuretic hormone secretion subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 264 (0.00%) 0 | 0 / 267 (0.00%) 0 |
| Thyroiditis subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 264 (0.00%) 0 | 3 / 267 (1.12%) 3 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------|----------------|-------------------|-------------------|
| Groin pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 7 / 267 (2.62%) |
| occurrences (all) | 1 | 1 | 7 |
| Flank pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 1 / 267 (0.37%) |
| occurrences (all) | 1 | 2 | 1 |
| Back pain | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 37 / 264 (14.02%) | 33 / 267 (12.36%) |
| occurrences (all) | 2 | 49 | 40 |
| Arthritis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 4 / 264 (1.52%) | 6 / 267 (2.25%) |
| occurrences (all) | 1 | 4 | 6 |
| Arthralgia | | | |
| subjects affected / exposed | 6 / 9 (66.67%) | 80 / 264 (30.30%) | 87 / 267 (32.58%) |
| occurrences (all) | 35 | 155 | 165 |
| Joint swelling | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 5 / 264 (1.89%) | 6 / 267 (2.25%) |
| occurrences (all) | 3 | 5 | 6 |
| Limb discomfort | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 2 / 267 (0.75%) |
| occurrences (all) | 1 | 0 | 3 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 5 / 264 (1.89%) | 1 / 267 (0.37%) |
| occurrences (all) | 2 | 5 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 8 / 264 (3.03%) | 3 / 267 (1.12%) |
| occurrences (all) | 0 | 11 | 3 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 3 / 264 (1.14%) | 5 / 267 (1.87%) |
| occurrences (all) | 2 | 5 | 6 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 4 / 264 (1.52%) | 8 / 267 (3.00%) |
| occurrences (all) | 0 | 4 | 9 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 28 / 264 (10.61%) | 32 / 267 (11.99%) |
| occurrences (all) | 0 | 36 | 68 |

| | | | |
|----------------------------------|----------------|-------------------|-------------------|
| Myalgia | | | |
| subjects affected / exposed | 4 / 9 (44.44%) | 37 / 264 (14.02%) | 43 / 267 (16.10%) |
| occurrences (all) | 6 | 83 | 71 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 9 / 264 (3.41%) | 7 / 267 (2.62%) |
| occurrences (all) | 0 | 9 | 7 |
| Osteopenia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 23 / 264 (8.71%) | 31 / 267 (11.61%) |
| occurrences (all) | 1 | 30 | 48 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 5 / 264 (1.89%) | 20 / 267 (7.49%) |
| occurrences (all) | 0 | 5 | 22 |
| Candida infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 0 / 267 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 13 / 264 (4.92%) | 18 / 267 (6.74%) |
| occurrences (all) | 0 | 13 | 20 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 6 / 267 (2.25%) |
| occurrences (all) | 1 | 3 | 8 |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Furuncle | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 264 (1.14%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Fungal skin infection | | | |

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|-------------------------------|----------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 2 / 267 (0.75%) |
| occurrences (all) | 1 | 1 | 2 |
| Folliculitis | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 8 / 264 (3.03%) | 14 / 267 (5.24%) |
| occurrences (all) | 5 | 10 | 19 |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 9 / 264 (3.41%) | 14 / 267 (5.24%) |
| occurrences (all) | 2 | 9 | 15 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 32 / 264 (12.12%) | 28 / 267 (10.49%) |
| occurrences (all) | 2 | 39 | 44 |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 2 / 267 (0.75%) |
| occurrences (all) | 1 | 2 | 3 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 3 / 267 (1.12%) |
| occurrences (all) | 1 | 2 | 3 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 12 / 267 (4.49%) |
| occurrences (all) | 1 | 3 | 15 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 10 / 264 (3.79%) | 18 / 267 (6.74%) |
| occurrences (all) | 1 | 11 | 20 |
| Postoperative wound infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 9 / 264 (3.41%) | 9 / 267 (3.37%) |
| occurrences (all) | 1 | 10 | 10 |
| Paronychia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 264 (1.14%) | 4 / 267 (1.50%) |
| occurrences (all) | 1 | 4 | 5 |
| Otitis media chronic | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Otitis media | | | |

| | | | |
|---|----------------|-------------------|-------------------|
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 264 (0.38%) | 1 / 267 (0.37%) |
| occurrences (all) | 1 | 1 | 1 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 4 / 264 (1.52%) | 8 / 267 (3.00%) |
| occurrences (all) | 1 | 4 | 10 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 9 / 264 (3.41%) | 17 / 267 (6.37%) |
| occurrences (all) | 4 | 10 | 30 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 2 / 264 (0.76%) | 2 / 267 (0.75%) |
| occurrences (all) | 1 | 3 | 2 |
| Viral rhinitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Viral pharyngitis | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 0 / 264 (0.00%) | 0 / 267 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 5 / 264 (1.89%) | 4 / 267 (1.50%) |
| occurrences (all) | 1 | 5 | 5 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 25 / 264 (9.47%) | 26 / 267 (9.74%) |
| occurrences (all) | 0 | 39 | 55 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 27 / 264 (10.23%) | 33 / 267 (12.36%) |
| occurrences (all) | 2 | 30 | 38 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 264 (1.14%) | 3 / 267 (1.12%) |
| occurrences (all) | 1 | 4 | 3 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 16 / 264 (6.06%) | 14 / 267 (5.24%) |
| occurrences (all) | 0 | 25 | 21 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 24 / 264 (9.09%) | 37 / 267 (13.86%) |
| occurrences (all) | 1 | 35 | 92 |

| | | | |
|--|---------------------|-----------------------|------------------------|
| Hypocalcaemia subjects affected / exposed occurrences (all) | 0 / 9 (0.00%) 0 | 4 / 264 (1.52%) 4 | 3 / 267 (1.12%) 3 |
| Hypokalaemia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 2 | 6 / 264 (2.27%) 7 | 15 / 267 (5.62%) 27 |
| Hyponatraemia subjects affected / exposed occurrences (all) | 2 / 9 (22.22%) 3 | 4 / 264 (1.52%) 5 | 17 / 267 (6.37%) 30 |
| Hypercholesterolaemia subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 4 / 264 (1.52%) 10 | 8 / 267 (3.00%) 14 |
| Iron deficiency subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 0 / 264 (0.00%) 0 | 2 / 267 (0.75%) 2 |
| Type 2 diabetes mellitus subjects affected / exposed occurrences (all) | 1 / 9 (11.11%) 1 | 5 / 264 (1.89%) 5 | 1 / 267 (0.37%) 1 |

| | | | |
|--|---------------------------|--|--|
| Non-serious adverse events | Part II PDR001 + D + T | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 27 / 27 (100.00%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Fibrous histiocytoma subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Basal cell carcinoma subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 | | |
| Vascular disorders Hot flush subjects affected / exposed occurrences (all) | 3 / 27 (11.11%) 4 | | |
| Superficial vein thrombosis subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |

| | | | |
|---|------------------------|--|--|
| Hypotension subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 | | |
| Lymphoedema subjects affected / exposed occurrences (all) | 3 / 27 (11.11%) 3 | | |
| Orthostatic hypotension subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 2 | | |
| Hypertension subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 2 | | |
| General disorders and administration site conditions | | | |
| Face oedema subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Fatigue subjects affected / exposed occurrences (all) | 11 / 27 (40.74%) 15 | | |
| Influenza like illness subjects affected / exposed occurrences (all) | 4 / 27 (14.81%) 5 | | |
| Non-cardiac chest pain subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 | | |
| Oedema subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 3 | | |
| Oedema due to cardiac disease subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Chills subjects affected / exposed occurrences (all) | 9 / 27 (33.33%) 44 | | |
| Axillary pain | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Asthenia | | | |
| subjects affected / exposed | 11 / 27 (40.74%) | | |
| occurrences (all) | 17 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 3 | | |
| Pain | | | |
| subjects affected / exposed | 5 / 27 (18.52%) | | |
| occurrences (all) | 6 | | |
| Pyrexia | | | |
| subjects affected / exposed | 23 / 27 (85.19%) | | |
| occurrences (all) | 99 | | |
| Xerosis | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Immune system disorders | | | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sarcoidosis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Reproductive system and breast disorders | | | |
| Ovarian cyst | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | | |
| occurrences (all) | 3 | | |
| Cough | | | |
| subjects affected / exposed | 12 / 27 (44.44%) | | |
| occurrences (all) | 15 | | |
| Epistaxis | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pneumonitis | | | |
| subjects affected / exposed | 4 / 27 (14.81%) | | |
| occurrences (all) | 5 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Disorientation | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bradyphrenia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--|-----------------|--|--|
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 7 / 27 (25.93%) | | |
| occurrences (all) | 12 | | |
| Blood testosterone decreased | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Amylase increased | | | |
| subjects affected / exposed | 4 / 27 (14.81%) | | |
| occurrences (all) | 6 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 5 / 27 (18.52%) | | |
| occurrences (all) | 13 | | |
| Blood albumin decreased | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 4 / 27 (14.81%) | | |
| occurrences (all) | 8 | | |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | | |
| occurrences (all) | 5 | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 9 / 27 (33.33%) | | |
| occurrences (all) | 13 | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 4 | | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Blood sodium decreased | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood thyroid stimulating hormone | | | |

| | | | |
|-------------------------------------|-----------------|--|--|
| decreased | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| C-reactive protein increased | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | | |
| occurrences (all) | 3 | | |
| Globulins increased | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Lipase increased | | | |
| subjects affected / exposed | 5 / 27 (18.52%) | | |
| occurrences (all) | 8 | | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Myoglobin blood increased | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | | |
| occurrences (all) | 4 | | |
| Transaminases increased | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Weight decreased | | | |
| subjects affected / exposed | 4 / 27 (14.81%) | | |
| occurrences (all) | 4 | | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 3 | | |
| Injury, poisoning and procedural complications | | | |
| Compression fracture | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Radiation skin injury | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |
| Anosmia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Aphasia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 2 | | |
| Syncope | | | |
| subjects affected / exposed | 4 / 27 (14.81%) | | |
| occurrences (all) | 4 | | |
| Peroneal nerve palsy | | | |

| | | | |
|--------------------------------------|------------------|--|--|
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 5 / 27 (18.52%) | | |
| occurrences (all) | 8 | | |
| Migraine | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Headache | | | |
| subjects affected / exposed | 8 / 27 (29.63%) | | |
| occurrences (all) | 18 | | |
| Dysgeusia | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | | |
| occurrences (all) | 3 | | |
| Dysaesthesia | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | | |
| occurrences (all) | 3 | | |
| Dizziness postural | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood and lymphatic system disorders | | | |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 3 | | |
| Anaemia | | | |
| subjects affected / exposed | 10 / 27 (37.04%) | | |
| occurrences (all) | 13 | | |
| Lymphopenia | | | |
| subjects affected / exposed | 4 / 27 (14.81%) | | |
| occurrences (all) | 11 | | |
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|-----------------------|--|--|
| Thrombocytopenia subjects affected / exposed occurrences (all) | 3 / 27 (11.11%) 7 | | |
| Neutropenia subjects affected / exposed occurrences (all) | 3 / 27 (11.11%) 11 | | |
| Ear and labyrinth disorders | | | |
| Ear congestion subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Ear pain subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Motion sickness subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Eye disorders | | | |
| Dry eye subjects affected / exposed occurrences (all) | 9 / 27 (33.33%) 9 | | |
| Myopia subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Iridocyclitis subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Ocular discomfort subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 2 | | |
| Papilloedema subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 | | |
| Vitreous cells subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Visual impairment | | | |

| | | | |
|----------------------------------|-----------------|--|--|
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Vision blurred | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Uveitis | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | | |
| occurrences (all) | 3 | | |
| Retinopathy | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Retinal haemorrhage | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Photophobia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Periorbital oedema | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Glossitis | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dry mouth | | | |
| subjects affected / exposed | 6 / 27 (22.22%) | | |
| occurrences (all) | 8 | | |

| | | | |
|-----------------------------|------------------|--|--|
| Nausea | | | |
| subjects affected / exposed | 8 / 27 (29.63%) | | |
| occurrences (all) | 19 | | |
| Constipation | | | |
| subjects affected / exposed | 7 / 27 (25.93%) | | |
| occurrences (all) | 10 | | |
| Cheilitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 5 / 27 (18.52%) | | |
| occurrences (all) | 10 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 9 / 27 (33.33%) | | |
| occurrences (all) | 14 | | |
| Vomiting | | | |
| subjects affected / exposed | 10 / 27 (37.04%) | | |
| occurrences (all) | 14 | | |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Trichoglossia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hepatobiliary disorders | | | |
| Hepatic cytolysis | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hepatic steatosis | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypertransaminasaemia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Hepatitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 2 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Dry skin | | | |
| subjects affected / exposed | 4 / 27 (14.81%) | | |
| occurrences (all) | 7 | | |
| Alopecia | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Eczema | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 3 | | |
| Erythema | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | | |
| occurrences (all) | 3 | | |
| Photosensitivity reaction | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Panniculitis | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Palmoplantar keratoderma | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 2 | | |

| | | | |
|-----------------------------|-----------------|--|--|
| Night sweats | | | |
| subjects affected / exposed | 4 / 27 (14.81%) | | |
| occurrences (all) | 5 | | |
| Ingrowing nail | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperkeratosis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Granuloma annulare | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Erythema nodosum | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 2 | | |
| Pruritus | | | |
| subjects affected / exposed | 8 / 27 (29.63%) | | |
| occurrences (all) | 12 | | |
| Skin disorder | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sensitive skin | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Seborrhoeic dermatitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash pruritic | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Stasis dermatitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|------------------------|--|--|
| Rash macular subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 3 | | |
| Rash erythematous subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 | | |
| Rash subjects affected / exposed occurrences (all) | 13 / 27 (48.15%) 20 | | |
| Psoriasis subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 4 | | |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 3 / 27 (11.11%) 3 | | |
| Urticaria subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 | | |
| Vitiligo subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 2 | | |
| Renal and urinary disorders | | | |
| Dysuria subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 | | |
| Haematuria subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Nocturia subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 2 | | |
| Acute kidney injury subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 2 | | |
| Endocrine disorders | | | |

| | | | |
|---|------------------|--|--|
| Hypophysitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 2 | | |
| Inappropriate antidiuretic hormone secretion | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Thyroiditis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Groin pain | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Flank pain | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Back pain | | | |
| subjects affected / exposed | 5 / 27 (18.52%) | | |
| occurrences (all) | 8 | | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Arthralgia | | | |
| subjects affected / exposed | 15 / 27 (55.56%) | | |
| occurrences (all) | 26 | | |
| Joint swelling | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 4 | | |
| Limb discomfort | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 2 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 3 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscular weakness | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Myalgia | | | |
| subjects affected / exposed | 8 / 27 (29.63%) | | |
| occurrences (all) | 11 | | |
| Neck pain | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | | |
| occurrences (all) | 4 | | |
| Osteopenia | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 6 / 27 (22.22%) | | |
| occurrences (all) | 11 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |

| | | | |
|----------------------------------|-----------------|--|--|
| Candida infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cellulitis | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 3 | | |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Furuncle | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Folliculitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 2 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | | |
| occurrences (all) | 4 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 27 (11.11%) | | |
| occurrences (all) | 3 | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sinusitis | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 2 | | |

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|---|----------------|--|--|
| Rhinitis | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Postoperative wound infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 27 (7.41%) | | |
| occurrences (all) | 4 | | |
| Paronychia | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Otitis media chronic | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Otitis media | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Viral rhinitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Viral pharyngitis | | | |
| subjects affected / exposed | 0 / 27 (0.00%) | | |
| occurrences (all) | 0 | | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 27 (3.70%) | | |
| occurrences (all) | 1 | | |

| | | | |
|--|----------------------|--|--|
| Urinary tract infection subjects affected / exposed occurrences (all) | 5 / 27 (18.52%) 5 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 7 / 27 (25.93%) 9 | | |
| Dehydration subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Hypophosphataemia subjects affected / exposed occurrences (all) | 4 / 27 (14.81%) 9 | | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 3 | | |
| Hypocalcaemia subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 2 | | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 3 | | |
| Hyponatraemia subjects affected / exposed occurrences (all) | 2 / 27 (7.41%) 2 | | |
| Hypercholesterolaemia subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 | | |
| Iron deficiency subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |
| Type 2 diabetes mellitus subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 27 January 2017 | <ul style="list-style-type: none">Removed double barrier contraception from the list of highly effective methods of contraception and clarified this removal from the exclusion criterion. |
| 07 March 2017 | <ul style="list-style-type: none">Updated criteria for DLT for Part 1.Added '≥ grade 3 AEs that were known to occur with dabrafenib, trametinib and/or spartalizumab, but cannot be controlled using the recommended product-specific management guidelines or lead to 50% of planned exposure to study medications'.Changed threshold for subjects with normal baseline AST and ALT values: 'AST or ALT > 8.0 × ULN' (grade 4 AST or ALT elevation' was subsequently removed)'Active infection requiring systemic antibiotic therapy within 2 weeks prior to start of study treatment'Added requirement for a local HIV testing at screening for subjects in Germany to exclusion criterionUpdated primary objective and endpoint for Part 2 to specifically mention the main two biomarkers of interest (PD-L1 levels and CD+8 cells). |
| 14 July 2017 | <ul style="list-style-type: none">Changes were made to pyrexia management guidelines based on the safety profile observed in the safety run-in (part 1) and feedback received from investigators upon review of safety data.Changes to improve data collection for radiotherapy events, central review using tumor response criteria based on guidelines for immunotherapy, ophthalmologic examination assessment frequency, and patient reported outcomes were implementedThe BRAF V600 testing method was clarified and language was added to reflect the AJCC edition 8 melanoma staging systemThe frequency of the data monitoring committee review of safety data was revised from 6 to 3-6 months to ensure appropriate safety monitoring |
| 14 August 2018 | <ul style="list-style-type: none">Aligned the contraception requirements during and after study treatment based on the dabrafenib Investigator's Brochure (IB) Edition 10 and trametinib IB Edition 9.The safety follow-up periods were aligned with the contraception requirements after study treatment had been discontinued.Revised individual subject unblinding requirements to limit the impact of unblinding on the scientific validity of the study resultsAdded a new exploratory objective and a corresponding endpoint to characterize the potential for TMB alone and in combination with PD-L1, or additional markers to identify subjects with an enhanced response to spartalizumab in combination with dabrafenib and trametinib versus placebo plus dabrafenib and trametinib.Updated withdrawal of consent to reflect European Economic Area General Data Protection Regulation requirements. Except for US and Japan, all biological samples not yet analyzed at the time of withdrawal were no longer to be used for analysis. |
| 08 March 2019 | <ul style="list-style-type: none">Adjusted the timing of the final PFS analysis and included an interim analysis for PFS based on revised assumptions on the delayed treatment effect.In order to achieve a statistical power of 80% based on a conservative assumption of a 5 months delayed treatment effect and followed by an effect of the same magnitude as assumed in the original protocol (i.e. HR=0.60), the number of PFS events for the final PFS analysis was increased from 246 to approximately 352 PFS events. Furthermore, an interim PFS analysis was introduced at approximately 260 PFS events.In addition, OS analysis was also revised based on the assumed 5 months delayed treatment effect. |

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| 13 October 2020 | <ul style="list-style-type: none"> • The primary objective of this amendment was to enable continuation of the study following the final PFS analysis, in order to characterize the overall survival benefit observed at the final PFS analysis. • Removal of the crossover schedule as it was no longer applicable as protocol defined criteria for crossover was not met. • Inclusion of all general recommendations already provided to the investigators in a letter dated 7-Apr-2020 to provide guidance on coronavirus disease-19 (COVID-19) related challenges that may affected the study protocol execution. • The contraception information was updated. |
| 18 January 2023 | <ul style="list-style-type: none"> • Revised the definition of end of study in section 4.3 of the protocol to include Post-Trial Access (PTA) program i.e., rollover protocol or a post study drug supply (PSDS) option for subjects still on study treatment and in the opinion of the investigator still deriving clinical benefit at the time of end of the study. • Updated safety information on hemophagocytic lymphohistiocytosis (HLH) and updated "dose modification and recommended clinical management guidelines" in the safety section including treatment resumption for recurrent grade 4 asymptomatic amylase or lipase elevation per UK Health Authority (MHRA) request. • A sub-section 2.7 related to public health emergency mitigation procedures was added. • Section 8.3 related to "Emergency unblinding of treatment assignment" was updated for clarification per Swissmedic feedback. • Language was updated to align with the latest Novartis protocol template (OneCTP version 5.0). |

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.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please go to <https://www.novctrd.com/#/> for complete trial results

Notes: