# Clinical trial results:
# A Multicenter, Double Blind, Randomized, Controlled Study of M7824 With Concurrent Chemoradiation Followed by M7824 Versus Concurrent Chemoradiation Plus Placebo Followed by Durvalumab in Participants With Unresectable Stage III Non-small Cell Lung Cancer

## Summary

| | |
|---|---|
| EudraCT number | 2018-003265-34 |
| Trial protocol | FR DE BE NL ES HU NO |
| Global end of trial date | 17 February 2023 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 21 December 2023 |
| First version publication date | 21 December 2023 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | MS200647_0005 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03840902 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Merck Healthcare KGaA, Darmstadt, Germany |
| Sponsor organisation address | Frankfurter Strasse 250, Darmstadt, Germany, 64293 |
| Public contact | Communication Centre, Merck Healthcare KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.com |
| Scientific contact | Communication Centre, Merck Healthcare KGaA, Darmstadt, Germany, +49 6151725200, service@merckgroup.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 | 17 February 2023 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 17 February 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

The main purpose of this study was to evaluate safety and efficacy in subjects treated with concomitant chemoradiation therapy (cCRT) plus M7824 followed by M7824 compared to cCRT plus placebo followed by durvalumab.

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 16 April 2019 |
| 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 | United States: 9 |
| Country: Number of subjects enrolled | Belgium: 2 |
| Country: Number of subjects enrolled | Czechia: 1 |
| Country: Number of subjects enrolled | France: 3 |
| Country: Number of subjects enrolled | Germany: 1 |
| Country: Number of subjects enrolled | Hungary: 1 |
| Country: Number of subjects enrolled | Netherlands: 2 |
| Country: Number of subjects enrolled | Poland: 3 |
| Country: Number of subjects enrolled | Russian Federation: 3 |
| Country: Number of subjects enrolled | Spain: 21 |
| Country: Number of subjects enrolled | Türkiye: 28 |
| Country: Number of subjects enrolled | China: 18 |
| Country: Number of subjects enrolled | Japan: 27 |
| Country: Number of subjects enrolled | Korea, Republic of: 9 |
| Country: Number of subjects enrolled | Taiwan: 5 |
| Country: Number of subjects enrolled | Argentina: 2 |
| Country: Number of subjects enrolled | Brazil: 8 |
| Country: Number of subjects enrolled | Australia: 10 |

| | |
|---|---|
| Worldwide total number of subjects | 153 |
| EEA total number of subjects | 34 |

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) | 70 |
| From 65 to 84 years | 82 |
| 85 years and over | 1 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

First subject signed informed consent: 16-Apr-2019, Clinical data cut-off: 21-Jul-2021.

### 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, Assessor |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | cCRT plus M7824 followed by M7824 |

Arm description:

Subjects received Concomitant Chemoradiotherapy (cCRT): Cisplatin/Etoposide [(50 milligrams per square meter (mg/m^2) of Cisplatin intravenously on Days 1, 8, 29, and 36 with 50 mg/m^2 intravenously of Etoposide daily on Days 1 to 5 and Days 29 to 33 during cCRT]; Carboplatin/Paclitaxel (carboplatin intravenously based on area under curve (AUC) 2 on Days 1, 8, 15, 22, 29, 36, and 43 with 45 mg/m^2 of Paclitaxel on Days 1, 8, 15, 22, 29, 36, and 43 during cCRT; Cisplatin/Pemetrexed (50 mg/m^2 of Cisplatin intravenously on Days 1, 8, 29, and 36 with 500 mg/m^2 of Pemetrexed intravenously on Days 1, 22, and 43 during cCRT concomitant with Intensity Modulated Radiation Therapy 5 (IMRT 5), fractions per week for about 6 weeks (Total 60 gray [Gy]) in combination with intravenous infusion of 1200 mg of M7824 every 2 weeks (q2w) during cCRT and up to 1 year after cCRT until unacceptable toxicity, confirmed disease progression assessed by investigator.

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

Dosage and administration details:

In combination with etoposide, subjects received cisplatin 50 mg/m^2 intravenously on Days 1, 8, 29, and 36 during cCRT. In combination with pemetrexed, subjects received cisplatin 75 mg/m2 intravenously on Days 1, 22, and 43 during cCRT.

| | |
|---|---|
| Investigational medicinal product name | carboplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received carboplatin intravenously based on area under curve (AUC) 2 on Day 1, Day 8, Day 15, Day 22, Day 29, Day 36, and Day 43 during cCRT.

| | |
|---|---|
| Investigational medicinal product name | M7824 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Sterile concentrate |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received intravenous infusion of 1200 mg of M7824 q2w during cCRT.

| | |
|---|---|
| Investigational medicinal product name | pemetrexed |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received pemetrexed at a dose of 500 mg/m^2 intravenously on Days 1, 22, and 43 during cCRT.

| | |
|---|---|
| Investigational medicinal product name | IMRT 5 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion, Radiopharmaceutical precursor |
| Routes of administration | Intravenous use, Not mentioned |

Dosage and administration details:

Subjects received IMRT 5 fractions per week for about 6 weeks (Total 60 gray [Gy]).

| | |
|---|---|
| Investigational medicinal product name | Etoposide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received etoposide 50 mg/m^2 intravenously daily on Day 1 to 5 and Day 29 to 33 during cCRT.

| | |
|---|---|
| Investigational medicinal product name | paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received paclitaxel intravenously at a dose of 45 mg/m^2 on Day 1, Day 8, Day 15, Day 22, Day 29, Day 36, and Day 43 during cCRT.

| | |
|---|---|
| **Arm title** | cCRT plus Placebo followed by Durvalumab |

Arm description:

Subjects received cCRT: Cisplatin/Etoposide [(50 mg/m^2) of Cisplatin intravenously on Days 1, 8, 29, and 36 with 50 mg/m^2 intravenously of Etoposide daily on Days 1 to 5 and Days 29 to 33 during cCRT]; Carboplatin/Paclitaxel, carboplatin intravenously based on AUC 2 on Days 1, 8, 15, 22, 29, 36, and 43 with 45 mg/m^2 of Paclitaxel on Days 1, 8, 15, 22, 29, 36, and 43 during cCRT; Cisplatin/Pemetrexed, 50 mg/m^2 of Cisplatin intravenously on Days 1, 8, 29, and 36 with 500 mg/m^2 of Pemetrexed intravenously on Days 1, 22, and 43 during cCRT concomitant with IMRT 5, Total 60 gy in combination with intravenous infusion of placebo matched to M7824 over 1 hour Q2W during cCRT followed by intravenous infusion of durvalumab 10 milligram per kilogram (mg/Kg) Q2W up to 1 year after cCRT until unacceptable toxicity, confirmed disease progression assessed by investigator.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Cisplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion, Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

In combination with etoposide, subjects received cisplatin 50 mg/m^2 intravenously on Days 1, 8, 29, and 36 during cCRT. In combination with pemetrexed, subjects received cisplatin 75 mg/m2 intravenously on Days 1, 22, and 43 during cCRT.

| | |
|---|---|
| Investigational medicinal product name | Etoposide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received etoposide 50 mg/m^2 intravenously daily on Day 1 to 5 and Day 29 to 33 during cCRT.

| | |
|---|---|
| Investigational medicinal product name | carboplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received carboplatin intravenously based on area under curve (AUC) 2 on Day 1, Day 8, Day 15, Day 22, Day 29, Day 36, and Day 43 during cCRT.

| | |
|---|---|
| Investigational medicinal product name | paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received paclitaxel intravenously at a dose of 45 mg/m^2 on Day 1, Day 8, Day 15, Day 22, Day 29, Day 36, and Day 43 during cCRT.

| | |
|---|---|
| Investigational medicinal product name | pemetrexed |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received pemetrexed at a dose of 500 mg/m^2 intravenously on Days 1, 22, and 43 during cCRT.

| | |
|---|---|
| Investigational medicinal product name | IMRT 5 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion, Radiopharmaceutical precursor |
| Routes of administration | Intravenous use, Not mentioned |

Dosage and administration details:

Subjects received IMRT 5 fractions per week for about 6 weeks (Total 60 gray [Gy]).

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Sterile concentrate |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received intravenous infusion of placebo matched to M7824 q2w during cCRT.

| | |
|---|---|
| Investigational medicinal product name | Durvalumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Sterile concentrate |
| Routes of administration | Intravenous use |

Dosage and administration details:

Subjects received intravenous infusion of durvalumab 10 mg/kg q2w up to 1 year.

| **Number of subjects in period 1** | cCRT plus M7824 followed by M7824 | cCRT plus Placebo followed by Durvalumab |
|---|---|---|
| Started | 75 | 78 |
| Treated | 74 | 77 |
| Completed | 74 | 77 |
| Not completed | 1 | 1 |
| Randomized but not treated | 1 | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | cCRT plus M7824 followed by M7824 |

Reporting group description:

Subjects received Concomitant Chemoradiotherapy (cCRT): Cisplatin/Etoposide [(50 milligrams per square meter (mg/m^2) of Cisplatin intravenously on Days 1, 8, 29, and 36 with 50 mg/m^2 intravenously of Etoposide daily on Days 1 to 5 and Days 29 to 33 during cCRT]; Carboplatin/Paclitaxel (carboplatin intravenously based on area under curve (AUC) 2 on Days 1, 8, 15, 22, 29, 36, and 43 with 45 mg/m^2 of Paclitaxel on Days 1, 8, 15, 22, 29, 36, and 43 during cCRT; Cisplatin/Pemetrexed (50 mg/m^2 of Cisplatin intravenously on Days 1, 8, 29, and 36 with 500 mg/m^2 of Pemetrexed intravenously on Days 1, 22, and 43 during cCRT concomitant with Intensity Modulated Radiation Therapy 5 (IMRT 5), fractions per week for about 6 weeks (Total 60 gray [Gy]) in combination with intravenous infusion of 1200 mg of M7824 every 2 weeks (q2w) during cCRT and up to 1 year after cCRT until unacceptable toxicity, confirmed disease progression assessed by investigator.

| Reporting group title | cCRT plus Placebo followed by Durvalumab |
|---|---|

Reporting group description:

Subjects received cCRT: Cisplatin/Etoposide [(50 mg/m^2) of Cisplatin intravenously on Days 1, 8, 29, and 36 with 50 mg/m^2 intravenously of Etoposide daily on Days 1 to 5 and Days 29 to 33 during cCRT]; Carboplatin/Paclitaxel, carboplatin intravenously based on AUC 2 on Days 1, 8, 15, 22, 29, 36, and 43 with 45 mg/m^2 of Paclitaxel on Days 1, 8, 15, 22, 29, 36, and 43 during cCRT; Cisplatin/Pemetrexed, 50 mg/m^2 of Cisplatin intravenously on Days 1, 8, 29, and 36 with 500 mg/m^2 of Pemetrexed intravenously on Days 1, 22, and 43 during cCRT concomitant with IMRT 5, Total 60 gy in combination with intravenous infusion of placebo matched to M7824 over 1 hour Q2W during cCRT followed by intravenous infusion of durvalumab 10 milligram per kilogram (mg/Kg) Q2W up to 1 year after cCRT until unacceptable toxicity, confirmed disease progression assessed by investigator.

| Reporting group values | cCRT plus M7824 followed by M7824 | cCRT plus Placebo followed by Durvalumab | Total |
|---|---|---|---|
| Number of subjects | 75 | 78 | 153 |
| Age categorical<br>Units: Subjects | | | |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 64.7 | 64.9 | |
| standard deviation | ± 9.35 | ± 8.94 | - |
| Sex: Female, Male<br>Units: subjects | | | |
| Female | 20 | 16 | 36 |
| Male | 55 | 62 | 117 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 25 | 34 | 59 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 1 | 0 | 1 |
| White | 48 | 41 | 89 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 1 | 3 | 4 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |

| | | | |
|---|---|---|---|
| Hispanic or Latino | 5 | 3 | 8 |
| Not Hispanic or Latino | 70 | 74 | 144 |
| Unknown or Not Reported | 0 | 1 | 1 |

## End points

### End points reporting groups

| Reporting group title | cCRT plus M7824 followed by M7824 |
|---|---|

Reporting group description:

Subjects received Concomitant Chemoradiotherapy (cCRT): Cisplatin/Etoposide [(50 milligrams per square meter (mg/m^2) of Cisplatin intravenously on Days 1, 8, 29, and 36 with 50 mg/m^2 intravenously of Etoposide daily on Days 1 to 5 and Days 29 to 33 during cCRT]; Carboplatin/Paclitaxel (carboplatin intravenously based on area under curve (AUC) 2 on Days 1, 8, 15, 22, 29, 36, and 43 with 45 mg/m^2 of Paclitaxel on Days 1, 8, 15, 22, 29, 36, and 43 during cCRT; Cisplatin/Pemetrexed (50 mg/m^2 of Cisplatin intravenously on Days 1, 8, 29, and 36 with 500 mg/m^2 of Pemetrexed intravenously on Days 1, 22, and 43 during cCRT concomitant with Intensity Modulated Radiation Therapy 5 (IMRT 5), fractions per week for about 6 weeks (Total 60 gray [Gy]) in combination with intravenous infusion of 1200 mg of M7824 every 2 weeks (q2w) during cCRT and up to 1 year after cCRT until unacceptable toxicity, confirmed disease progression assessed by investigator.

| Reporting group title | cCRT plus Placebo followed by Durvalumab |
|---|---|

Reporting group description:

Subjects received cCRT: Cisplatin/Etoposide [(50 mg/m^2) of Cisplatin intravenously on Days 1, 8, 29, and 36 with 50 mg/m^2 intravenously of Etoposide daily on Days 1 to 5 and Days 29 to 33 during cCRT]; Carboplatin/Paclitaxel, carboplatin intravenously based on AUC 2 on Days 1, 8, 15, 22, 29, 36, and 43 with 45 mg/m^2 of Paclitaxel on Days 1, 8, 15, 22, 29, 36, and 43 during cCRT; Cisplatin/Pemetrexed, 50 mg/m^2 of Cisplatin intravenously on Days 1, 8, 29, and 36 with 500 mg/m^2 of Pemetrexed intravenously on Days 1, 22, and 43 during cCRT concomitant with IMRT 5, Total 60 gy in combination with intravenous infusion of placebo matched to M7824 over 1 hour Q2W during cCRT followed by intravenous infusion of durvalumab 10 milligram per kilogram (mg/Kg) Q2W up to 1 year after cCRT until unacceptable toxicity, confirmed disease progression assessed by investigator.

### Primary: Progression-Free Survival (PFS) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by Investigator

| End point title | Progression-Free Survival (PFS) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by Investigator[1] |
|---|---|

End point description:

PFS was defined as the time from randomization to the date of first documentation of disease progression (PD) or death due to any cause, whichever occurred first. PD: At least a 20 percent (%) increase in the sum of the longest diameter (SLD) taking as reference the smallest SLD recorded from baseline or the appearance of 1 or more new lesions. PFS was analyzed by using the Kaplan-Meier method. Full Analysis Set (FAS) included all subjects who were randomized to study treatment.

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

End point timeframe:

Time from randomization to the date of first documentation of PD or death, assessed approximately up to 27 months

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistics was planned for this endpoint.

| End point values | cCRT plus M7824 followed by M7824 | cCRT plus Placebo followed by Durvalumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 78 | | |
| Units: months | | | | |
| median (full range (min-max)) | 3.7 (1.9 to 5.6) | 3.7 (1.8 to 3.9) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects with Treatment-Emergent Adverse Events (TEAEs) and Treatment-Related Adverse Events

| End point title | Number of Subjects with Treatment-Emergent Adverse Events (TEAEs) and Treatment-Related Adverse Events |
|---|---|

End point description:

Adverse Event (AE) was defined any untoward medical occurrence in a subject administered with a study drug, which does not necessarily have a causal relationship with this treatment. Serious AE was defined AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial/prolonged inpatient hospitalization; congenital anomaly/birth defect. TEAEs: TEAEs was defined as events with onset date or worsening during the on-treatment period. TEAEs included serious AEs and non-serious AEs. Treatment-related TEAEs: reasonably related to the study intervention. Safety (SAF) Analysis Set included all subjects who were administered any dose of any study intervention.

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

End point timeframe:

Time from randomization up to data cut off (assessed up to 27 months)

| End point values | cCRT plus M7824 followed by M7824 | cCRT plus Placebo followed by Durvalumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 74 | 77 | | |
| Units: subjects | | | | |
| TEAEs | 70 | 74 | | |
| Immunotherapy related TEAE | 48 | 48 | | |
| Cisplatin/etoposide chemotherapy related TEAE | 7 | 11 | | |
| Carboplatin/paclitaxel chemotherapy related TEAE | 46 | 47 | | |
| Cisplatin/pemetrexed chemotherapy related TEAE | 15 | 11 | | |
| Radiotherapy related TEAE | 59 | 60 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Immediate Observed Serum Concentration at End of Infusion (Ceoi) of M7824

| End point title | Immediate Observed Serum Concentration at End of Infusion (Ceoi) of M7824 |
|---|---|

End point description:

Ceoi is the serum concentration observed immediately at the end of infusion. This was taken directly from the observed M7824 concentration-time data. Based on recommendations by an external Independent Data Monitoring Committee (IDMC), Sponsor decided to discontinue this clinical study. Subsequently, the data for this outcome measure was not collected and analyzed.

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

End point timeframe:

Pre-dose, 30 minutes after end of infusion on Day 1, 15, 29, 57, 85, 127, 157, 343

| **End point values** | cCRT plus M7824 followed by M7824 | cCRT plus Placebo followed by Durvalumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[2] | 0[3] | | |
| Units: microgram per milliliter (mcg/mL) | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[2] - Data was not collected and analyzed.

[3] - Data was not collected and analyzed.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Response (DOR) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) as Assessed by Investigator

| End point title | Duration of Response (DOR) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) as Assessed by Investigator |
|---|---|

End point description:

DOR was defined for subjects with confirmed response, as the time from first documentation of objective response (Complete Response [CR] or Partial Response [PR]) to the date of first documentation of progression disease (PD) or death due to any cause, whichever occurred first. CR: Disappearance of all evidence of target and non-target lesions. PR: At least 30% reduction from baseline in the SLD of all lesions. PD: At least a 20 percent (%) increase in the SLD, taking as reference the smallest SLD recorded from baseline or the appearance of 1 or more new lesions. DOR was determined according to RECIST v1.1 and assessed by IRC. Results were calculated based on Kaplan-Meier estimates.

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

End point timeframe:

Time from first documentation of objective response to the date of first documentation of PD or death due to any cause, assessed approximately up to 27 months

| End point values | cCRT plus M7824 followed by M7824 | cCRT plus Placebo followed by Durvalumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[4] | 0[5] | | |
| Units: subjects | | | | |

Notes:

[4] - Due to early termination of the study, the data for this outcome measure was not collected.

[5] - Due to early termination of the study, the data for this outcome measure was not collected.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Survival (OS)

| End point title | Overall Survival (OS) |
|---|---|

End point description:

Overall Survival was defined as the time from randomization to the date of death due to any cause. The overall survival was analyzed by using the Kaplan-Meier method. FAS included all subjects who were randomized to study treatment.

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

End point timeframe:

Time from randomization to the date of death due to any cause, assessed up to 27 months

| End point values | cCRT plus M7824 followed by M7824 | cCRT plus Placebo followed by Durvalumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 78 | | |
| Units: months | | | | |
| median (full range (min-max)) | 4.6 (0.1 to 22.3) | 4.3 (0.3 to 22.7) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Objective Response Rate (ORR) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) as Assessed by Investigator

| End point title | Objective Response Rate (ORR) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) as Assessed by Investigator |
|---|---|

End point description:

ORR was defined as the percentage of subjects who had achieved complete response (CR) or partial response (PR) as the best overall response according to RECIST v1.1as adjudicated by the Investigator. CR: Complete Response (CR) defined as disappearance of all target and non-target lesions and any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. Partial response (PR) defined as at least a 30% decrease in the sum of diameters of target lesions. FAS included all subjects who were randomized to study treatment.

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

End point timeframe:

Time from randomization up to data cut off (assessed up to 27 months)

| **End point values** | cCRT plus M7824 followed by M7824 | cCRT plus Placebo followed by Durvalumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 78 | | |
| Units: percentage of subjects | | | | |
| number (confidence interval 95%) | 29.3 (19.4 to 41.0) | 32.1 (21.9 to 43.6) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Positive Antidrug Antibodies (ADA)

| End point title | Number of Subjects With Positive Antidrug Antibodies (ADA) |
|---|---|

End point description:

Serum samples were analyzed by a validated assay method to detect the presence of antidrug antibodies (ADA). Number of subjects with positive ADA were reported. Based on recommendations by an external Independent Data Monitoring Committee (IDMC), Sponsor decided to discontinue this clinical study. Subsequently, the data for this outcome measure was not collected and analyzed.

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

End point timeframe:

Time from randomization up to data cut off (assessed up to 27 months)

| **End point values** | cCRT plus M7824 followed by M7824 | cCRT plus Placebo followed by Durvalumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[6] | 0[7] | | |
| Units: subjects | | | | |
| number (not applicable) | | | | |

Notes:

[6] - Data was not collected and analyzed.

[7] - Data was not collected and analyzed.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Serum Concentration Immediately Before Next Dosing (Ctrough) of M7824

| End point title | Serum Concentration Immediately Before Next Dosing (Ctrough) of M7824 |
|---|---|

End point description:

Ctrough was the serum concentration observed immediately before next dosing. Based on recommendations by an external Independent Data Monitoring Committee (IDMC), Sponsor decided to discontinue this clinical study. Subsequently, the data for this outcome measure was not collected and analyzed.

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

End point timeframe:

Pre-dose, 30 minutes after end of infusion on Day 1, 15, 29, 57, 85, 127, 157, 343

| **End point values** | cCRT plus M7824 followed by M7824 | cCRT plus Placebo followed by Durvalumab | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[8] | 0[9] | | |
| Units: mcg/mL | | | | |
| geometric mean (geometric coefficient of variation) | () | () | | |

Notes:

[8] - Data was not collected and analyzed.

[9] - Data was not collected and analyzed.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Time from randomization up to data cut off (assessed up to 27 months)

Adverse event reporting additional description:

Safety (SAF) Analysis Set included all participants who were administered any dose of any study intervention.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 24.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | cCRT plus Placebo followed by Durvalumab |

Reporting group description:

Subjects received cCRT: Cisplatin/Etoposide [(50 mg/m^2) of Cisplatin intravenously on Days 1, 8, 29, and 36 with 50 mg/m^2 intravenously of Etoposide daily on Days 1 to 5 and Days 29 to 33 during cCRT]; Carboplatin/Paclitaxel, carboplatin intravenously based on AUC 2 on Days 1, 8, 15, 22, 29, 36, and 43 with 45 mg/m^2 of Paclitaxel on Days 1, 8, 15, 22, 29, 36, and 43 during cCRT; Cisplatin/Pemetrexed, 50 mg/m^2 of Cisplatin intravenously on Days 1, 8, 29, and 36 with 500 mg/m^2 of Pemetrexed intravenously on Days 1, 22, and 43 during cCRT concomitant with IMRT 5, Total 60 gy in combination with intravenous infusion of placebo matched to M7824 over 1 hour Q2W during cCRT followed by intravenous infusion of durvalumab 10 milligram per kilogram (mg/Kg) Q2W up to 1 year after cCRT until unacceptable toxicity, confirmed disease progression assessed by investigator.

| | |
|---|---|
| Reporting group title | cCRT plus M7824 followed by M7824 |

Reporting group description:

Subjects received Concomitant Chemoradiotherapy (cCRT): Cisplatin/Etoposide [(50 milligrams per square meter (mg/m^2) of Cisplatin intravenously on Days 1, 8, 29, and 36 with 50 mg/m^2 intravenously of Etoposide daily on Days 1 to 5 and Days 29 to 33 during cCRT]; Carboplatin/Paclitaxel (carboplatin intravenously based on area under curve (AUC) 2 on Days 1, 8, 15, 22, 29, 36, and 43 with 45 mg/m^2 of Paclitaxel on Days 1, 8, 15, 22, 29, 36, and 43 during cCRT; Cisplatin/Pemetrexed (50 mg/m^2 of Cisplatin intravenously on Days 1, 8, 29, and 36 with 500 mg/m^2 of Pemetrexed intravenously on Days 1, 22, and 43 during cCRT concomitant with Intensity Modulated Radiation Therapy 5 (IMRT 5), fractions per week for about 6 weeks (Total 60 gray [Gy]) in combination with intravenous infusion of 1200 mg of M7824 every 2 weeks (q2w) during cCRT and up to 1 year after cCRT until unacceptable toxicity, confirmed disease progression assessed by investigator.

| **Serious adverse events** | cCRT plus Placebo followed by Durvalumab | cCRT plus M7824 followed by M7824 | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 31 / 77 (40.26%) | 43 / 74 (58.11%) | |
| number of deaths (all causes) | 5 | 13 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Bowen's disease | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to central nervous system | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transitional cell carcinoma | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Hypotension | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Disease progression | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Pyrexia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 1 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mucosal inflammation | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Immune system disorders | | | |
| Contrast media allergy | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumonitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 6 / 77 (7.79%) | 5 / 74 (6.76%) | |
| occurrences causally related to treatment / all | 6 / 9 | 5 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune-mediated lung disease | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hiccups | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Atelectasis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Bronchial haemorrhage | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Dyspnoea | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 3 / 74 (4.05%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Pulmonary embolism | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glomerular filtration rate decreased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutrophil count decreased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Femur fracture | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radiation mucositis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radiation oesophagitis | | | |

| | | | |
|---|---|---|---|
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 3 / 74 (4.05%) | |
| occurrences causally related to treatment / all | 2 / 2 | 3 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radiation pneumonitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 3 / 74 (4.05%) | |
| occurrences causally related to treatment / all | 2 / 2 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Cardiac disorders** | | | |
| Atrioventricular block complete | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Myocardial infarction | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericardial effusion | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brain stem haemorrhage | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Neuropathy peripheral | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thoracic outlet syndrome | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 4 / 74 (5.41%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelosuppression | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukopenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspepsia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal vascular malformation haemorrhagic | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoidal haemorrhage | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 5 / 74 (6.76%) | |
| occurrences causally related to treatment / all | 0 / 0 | 5 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal haemorrhage | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophagitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 3 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 3 / 74 (4.05%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Impaired gastric emptying | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Immune-mediated hepatitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Pemphigoid | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erythema multiforme | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erythema | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthralgia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Device related infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Parainfluenzae virus infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacteraemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 3 / 74 (4.05%) | |
| occurrences causally related to treatment / all | 0 / 4 | 1 / 5 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Pneumonia bacterial | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary sepsis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |

| | | | |
|---|---|---|---|
| Sepsis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 3 / 74 (4.05%) | |
| occurrences causally related to treatment / all | 0 / 1 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Urinary tract infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hypocalcaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypomagnesaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malnutrition | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | cCRT plus Placebo followed by Durvalumab | cCRT plus M7824 followed by M7824 | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 72 / 77 (93.51%) | 68 / 74 (91.89%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Keratoacanthoma | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 4 / 74 (5.41%) | |
| occurrences (all) | 0 | 5 | |
| Leukaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Skin papilloma | | | |

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|---|---|---|---|
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Vascular disorders | | | |
| Phlebitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Orthostatic hypotension | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Intermittent claudication | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Phlebitis superficial | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypertension | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 3 / 74 (4.05%) | |
| occurrences (all) | 2 | 3 | |
| Deep vein thrombosis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Hypotension | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 4 / 74 (5.41%) | |
| occurrences (all) | 5 | 4 | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Chills | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 1 / 74 (1.35%) | |
| occurrences (all) | 4 | 1 | |
| Asthenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 6 / 77 (7.79%) | 13 / 74 (17.57%) | |
| occurrences (all) | 6 | 19 | |
| Catheter site pruritus | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Chest discomfort | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Chest pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Fatigue | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 14 / 77 (18.18%) | 5 / 74 (6.76%) | |
| occurrences (all) | 15 | 5 | |
| Gait disturbance | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Generalised oedema | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences (all) | 1 | 1 | |
| Hyperthermia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | | |
| occurrences (all) | 0 | 1 | | |
| Infusion site extravasation | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | | |
| occurrences (all) | 0 | 1 | | |
| Infusion site reaction | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | | |
| occurrences (all) | 0 | 1 | | |
| Malaise | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 6 / 77 (7.79%) | 5 / 74 (6.76%) | | |
| occurrences (all) | 6 | 6 | | |
| Mucosal haemorrhage | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | | |
| occurrences (all) | 0 | 1 | | |
| Mucosal inflammation | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 5 / 74 (6.76%) | | |
| occurrences (all) | 3 | 6 | | |
| Oedema peripheral | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | | |
| occurrences (all) | 1 | 0 | | |
| Pain | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | | |
| occurrences (all) | 0 | 2 | | |
| Pyrexia | | | | |
| alternative dictionary used: MedDRA 24.0 | | | | |
| subjects affected / exposed | 10 / 77 (12.99%) | 18 / 74 (24.32%) | | |
| occurrences (all) | 11 | 22 | | |

| | | | |
|---|---|---|---|
| Feeling hot<br>alternative dictionary used: MedDRA 24.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 77 (0.00%)<br>0 | 1 / 74 (1.35%)<br>1 | |
| Immune system disorders<br>Hypersensitivity<br>alternative dictionary used: MedDRA 24.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 77 (0.00%)<br>0 | 1 / 74 (1.35%)<br>1 | |
| Reproductive system and breast disorders<br>Benign prostatic hyperplasia<br>alternative dictionary used: MedDRA 24.0<br>subjects affected / exposed<br>occurrences (all) | 1 / 77 (1.30%)<br>1 | 0 / 74 (0.00%)<br>0 | |
| Breast pain<br>alternative dictionary used: MedDRA 24.0<br>subjects affected / exposed<br>occurrences (all) | 1 / 77 (1.30%)<br>1 | 0 / 74 (0.00%)<br>0 | |
| Erectile dysfunction<br>alternative dictionary used: MedDRA 24.0<br>subjects affected / exposed<br>occurrences (all) | 0 / 77 (0.00%)<br>0 | 1 / 74 (1.35%)<br>1 | |
| Erection increased<br>alternative dictionary used: MedDRA 24.0<br>subjects affected / exposed<br>occurrences (all) | 1 / 77 (1.30%)<br>1 | 0 / 74 (0.00%)<br>0 | |
| Respiratory, thoracic and mediastinal disorders<br>Atelectasis<br>alternative dictionary used: MedDRA 24.0<br>subjects affected / exposed<br>occurrences (all) | 1 / 77 (1.30%)<br>1 | 1 / 74 (1.35%)<br>1 | |
| Bronchitis chronic<br>alternative dictionary used: MedDRA 24.0 | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Epistaxis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 13 / 74 (17.57%) | |
| occurrences (all) | 2 | 16 | |
| Respiratory distress | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Dyspnoea | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 7 / 77 (9.09%) | 3 / 74 (4.05%) | |
| occurrences (all) | 7 | 4 | |
| Dysphonia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cough | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 14 / 77 (18.18%) | 15 / 74 (20.27%) | |
| occurrences (all) | 16 | 15 | |
| Chronic obstructive pulmonary disease | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Haemoptysis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 7 / 74 (9.46%) | |
| occurrences (all) | 3 | 9 | |
| Hiccups | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 6 / 77 (7.79%) | 6 / 74 (8.11%) | |
| occurrences (all) | 6 | 9 | |

| | | | |
|---|---|---|---|
| Hypoxia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Interstitial lung disease | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 3 | |
| Oropharyngeal pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 2 / 74 (2.70%) | |
| occurrences (all) | 3 | 2 | |
| Pleural effusion | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Pleurisy | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pneumonitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 10 / 77 (12.99%) | 4 / 74 (5.41%) | |
| occurrences (all) | 12 | 4 | |
| Pneumothorax | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Productive cough | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 4 / 74 (5.41%) | |
| occurrences (all) | 3 | 6 | |
| Pulmonary embolism | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 77 (2.60%) | 2 / 74 (2.70%) | |
| occurrences (all) | 2 | 2 | |
| Dyspnoea exertional | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Rhinorrhoea | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences (all) | 1 | 1 | |
| Anxiety disorder | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Delirium | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Depression | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Insomnia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 9 / 77 (11.69%) | 9 / 74 (12.16%) | |
| occurrences (all) | 11 | 10 | |
| Product issues | | | |
| Device malfunction | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Investigations | | | |
| Activated partial thromboplastin time prolonged | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Alanine aminotransferase increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 9 / 77 (11.69%) | 6 / 74 (8.11%) | |
| occurrences (all) | 11 | 10 | |
| Alpha hydroxybutyrate dehydrogenase increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Amylase increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 5 / 74 (6.76%) | |
| occurrences (all) | 3 | 11 | |
| Anti-transglutaminase antibody increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Aspartate aminotransferase increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 7 / 77 (9.09%) | 6 / 74 (8.11%) | |
| occurrences (all) | 11 | 7 | |
| Blood alkaline phosphatase increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Blood bilirubin increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 77 (3.90%) | 3 / 74 (4.05%) | |
| occurrences (all) | 5 | 4 | |
| Blood cholesterol increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 1 / 74 (1.35%) | |
| occurrences (all) | 4 | 1 | |
| Blood creatine increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Blood creatine phosphokinase increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 4 / 74 (5.41%) | |
| occurrences (all) | 2 | 8 | |
| Blood creatinine increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 4 / 74 (5.41%) | |
| occurrences (all) | 4 | 4 | |
| Blood glucose increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 3 | |
| Blood lactate dehydrogenase increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 2 | |
| Blood thyroid stimulating hormone increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences (all) | 1 | 1 | |
| Blood triglycerides increased<br>alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood urea increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 5 / 77 (6.49%) | 2 / 74 (2.70%) | |
| occurrences (all) | 9 | 5 | |
| Brain natriuretic peptide increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| C-reactive protein increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 1 / 74 (1.35%) | |
| occurrences (all) | 2 | 2 | |
| Transaminases increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Gamma-glutamyltransferase increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 7 / 77 (9.09%) | 5 / 74 (6.76%) | |
| occurrences (all) | 13 | 7 | |
| Gastric pH decreased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Glomerular filtration rate decreased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 2 | |
| Hepatic enzyme increased<br>alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|---|
| Lipase increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 8 / 74 (10.81%) | |
| occurrences (all) | 1 | 9 | |
| Lung diffusion test decreased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Lymphocyte count decreased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 13 / 77 (16.88%) | 11 / 74 (14.86%) | |
| occurrences (all) | 23 | 16 | |
| Neutrophil count decreased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 20 / 77 (25.97%) | 17 / 74 (22.97%) | |
| occurrences (all) | 36 | 28 | |
| Platelet count decreased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 13 / 77 (16.88%) | 11 / 74 (14.86%) | |
| occurrences (all) | 21 | 16 | |
| Procalcitonin increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Protein total decreased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Prothrombin time prolonged | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 2 | |
| Pulmonary function test decreased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 77 (2.60%) | 1 / 74 (1.35%) | |
| occurrences (all) | 2 | 1 | |
| SARS-CoV-2 test positive | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Total bile acids increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fibrin D dimer increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| White blood cell count increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| White blood cell count decreased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 29 / 77 (37.66%) | 24 / 74 (32.43%) | |
| occurrences (all) | 59 | 37 | |
| Weight increased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Weight decreased | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 8 / 77 (10.39%) | 8 / 74 (10.81%) | |
| occurrences (all) | 8 | 9 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fibula fracture | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infusion related reaction | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 2 / 74 (2.70%) | |
| occurrences (all) | 3 | 2 | |
| Pelvic fracture | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Radiation fibrosis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Radiation fibrosis - lung | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Radiation mucositis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Radiation oesophagitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 13 / 77 (16.88%) | 13 / 74 (17.57%) | |
| occurrences (all) | 15 | 13 | |
| Radiation pneumonitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 9 / 77 (11.69%) | 7 / 74 (9.46%) | |
| occurrences (all) | 12 | 7 | |

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|---|---|---|---|
| Radiation skin injury | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 10 / 77 (12.99%) | 5 / 74 (6.76%) | |
| occurrences (all) | 10 | 5 | |
| Spinal compression fracture | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Thermal burn | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 3 | |
| Supraventricular extrasystoles | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Myocardial ischaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Palpitations | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Pericardial effusion | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Sinus tachycardia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 77 (2.60%) | 1 / 74 (1.35%) | |
| occurrences (all) | 2 | 1 | |
| Atrial fibrillation | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 2 / 74 (2.70%) | |
| occurrences (all) | 1 | 2 | |
| Supraventricular tachycardia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tachycardia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 1 / 74 (1.35%) | |
| occurrences (all) | 2 | 1 | |
| Nervous system disorders | | | |
| Tremor | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Cerebral microhaemorrhage | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Dizziness | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 5 / 77 (6.49%) | 3 / 74 (4.05%) | |
| occurrences (all) | 5 | 3 | |
| Syncope | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 1 / 74 (1.35%) | |
| occurrences (all) | 2 | 1 | |
| Somnolence | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Peripheral sensory neuropathy | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Neuropathy peripheral | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 2 / 74 (2.70%) | |
| occurrences (all) | 1 | 2 | |
| Headache | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 2 / 74 (2.70%) | |
| occurrences (all) | 5 | 2 | |
| Dysgeusia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 2 / 74 (2.70%) | |
| occurrences (all) | 1 | 2 | |
| Dizziness postural | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dizziness exertional | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 32 / 77 (41.56%) | 38 / 74 (51.35%) | |
| occurrences (all) | 53 | 49 | |
| Febrile neutropenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Lymphopenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 4 / 74 (5.41%) | |
| occurrences (all) | 3 | 4 | |
| Leukopenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 10 / 77 (12.99%) | 9 / 74 (12.16%) | |
| occurrences (all) | 12 | 13 | |
| Iron deficiency anaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Neutropenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 15 / 77 (19.48%) | 20 / 74 (27.03%) | |
| occurrences (all) | 18 | 27 | |
| Pancytopenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences (all) | 2 | 1 | |
| Thrombocytopenia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 7 / 77 (9.09%) | 11 / 74 (14.86%) | |
| occurrences (all) | 8 | 16 | |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tinnitus | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 0 / 74 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Abdominal pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 1 / 74 (1.35%) | |
| occurrences (all) | 2 | 1 | |
| Gingival pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Abdominal rigidity | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Anal fissure | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ascites | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Colitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 3 / 74 (4.05%) | |
| occurrences (all) | 1 | 3 | |
| Constipation | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

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|---|---|---|---|
| subjects affected / exposed | 34 / 77 (44.16%) | 23 / 74 (31.08%) | |
| occurrences (all) | 43 | 26 | |
| Dental caries | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Diarrhoea | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 12 / 77 (15.58%) | 12 / 74 (16.22%) | |
| occurrences (all) | 13 | 14 | |
| Dry mouth | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 3 / 74 (4.05%) | |
| occurrences (all) | 0 | 3 | |
| Dyspepsia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 5 / 74 (6.76%) | |
| occurrences (all) | 4 | 5 | |
| Dysphagia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 5 / 77 (6.49%) | 9 / 74 (12.16%) | |
| occurrences (all) | 5 | 10 | |
| Gastric ulcer | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Gastritis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 3 / 74 (4.05%) | |
| occurrences (all) | 2 | 3 | |
| Gastrooesophageal reflux disease | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 5 / 77 (6.49%) | 2 / 74 (2.70%) | |
| occurrences (all) | 5 | 2 | |

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|---|---|---|---|
| Gingival bleeding | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Abdominal pain upper | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 3 / 74 (4.05%) | |
| occurrences (all) | 0 | 3 | |
| Haematemesis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Mouth ulceration | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Nausea | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 29 / 77 (37.66%) | 26 / 74 (35.14%) | |
| occurrences (all) | 35 | 29 | |
| Odynophagia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 6 / 77 (7.79%) | 5 / 74 (6.76%) | |
| occurrences (all) | 7 | 6 | |
| Oesophageal ulcer | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Oesophagitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 24 / 77 (31.17%) | 15 / 74 (20.27%) | |
| occurrences (all) | 25 | 15 | |
| Proctalgia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Rectal haemorrhage | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 3 / 74 (4.05%) | |
| occurrences (all) | 0 | 3 | |
| Retching | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Stomatitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 9 / 74 (12.16%) | |
| occurrences (all) | 3 | 9 | |
| Vomiting | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 6 / 77 (7.79%) | 9 / 74 (12.16%) | |
| occurrences (all) | 7 | 12 | |
| Haematochezia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Hepatobiliary disorders | | | |
| Bile duct stone | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Drug-induced liver injury | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypertransaminasaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Immune-mediated hepatitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis acneiform | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 2 / 74 (2.70%) | |
| occurrences (all) | 5 | 2 | |
| Dermatitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences (all) | 1 | 1 | |
| Blister | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Alopecia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 7 / 77 (9.09%) | 6 / 74 (8.11%) | |
| occurrences (all) | 7 | 6 | |
| Actinic keratosis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Dry skin | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 2 / 74 (2.70%) | |
| occurrences (all) | 2 | 2 | |
| Pruritus | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

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|---|---|---|---|
| subjects affected / exposed | 8 / 77 (10.39%) | 13 / 74 (17.57%) | |
| occurrences (all) | 8 | 18 | |
| Pigmentation disorder | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pemphigoid | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Palmar-plantar erythrodysaesthesia syndrome | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Neurodermatitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Miliaria | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Lichenoid keratosis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Erythema multiforme | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Erythema | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 5 / 74 (6.76%) | |
| occurrences (all) | 1 | 7 | |

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|---|---|---|---|
| Eczema | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 3 / 74 (4.05%) | |
| occurrences (all) | 0 | 3 | |
| Psoriasis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 2 | |
| Rash | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 6 / 77 (7.79%) | 19 / 74 (25.68%) | |
| occurrences (all) | 7 | 25 | |
| Rash erythematous | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Skin toxicity | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Skin reaction | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Rash maculo-papular | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 4 / 74 (5.41%) | |
| occurrences (all) | 1 | 4 | |
| Rash macular | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Renal and urinary disorders | | | |

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|---|---|---|---|
| Haematuria | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences (all) | 2 | 1 | |
| Pollakiuria | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Proteinuria | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Renal failure | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Acute kidney injury | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Cystitis noninfective | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Dysuria | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Endocrine disorders | | | |
| Hypopituitarism | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypothyroidism | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 6 / 77 (7.79%) | 2 / 74 (2.70%) | |
| occurrences (all) | 6 | 2 | |
| Thyroiditis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hyperthyroidism | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 7 / 77 (9.09%) | 4 / 74 (5.41%) | |
| occurrences (all) | 7 | 4 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 7 / 74 (9.46%) | |
| occurrences (all) | 3 | 7 | |
| Arthritis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences (all) | 1 | 1 | |
| Myositis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Myalgia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 3 / 74 (4.05%) | |
| occurrences (all) | 1 | 3 | |
| Musculoskeletal stiffness | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal chest pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Intervertebral disc protrusion | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Haemarthrosis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Flank pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Back pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 6 / 74 (8.11%) | |
| occurrences (all) | 4 | 6 | |
| Neck pain | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Pain in extremity | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 3 / 74 (4.05%) | |
| occurrences (all) | 0 | 3 | |
| Rotator cuff syndrome | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Osteoporosis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |

| | | | |
|---|---|---|---|
| Infections and infestations | | | |
| Bacteraemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Molluscum contagiosum | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| COVID-19 | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Cystitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Cytomegalovirus infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Device related infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Empyema | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Folliculitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 4 | |
| Fungal skin infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Gastroenteritis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Gingivitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Herpes zoster | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 2 / 74 (2.70%) | |
| occurrences (all) | 0 | 2 | |
| Infectious pleural effusion | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Influenza | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Lower respiratory tract infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Bronchitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Nasopharyngitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences (all) | 1 | 1 | |

| | | | |
|---|---|---|---|
| Tinea infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Oesophageal infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Onychomycosis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Oral candidiasis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences (all) | 1 | 1 | |
| Oral fungal infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Peri-implantitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Periodontitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences (all) | 1 | 1 | |
| Pharyngotonsillitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Pneumonia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 77 (3.90%) | 8 / 74 (10.81%) | |
| occurrences (all) | 3 | 9 | |
| Post-acute COVID-19 syndrome | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pseudomembranous colitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Respiratory tract infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 2 / 74 (2.70%) | |
| occurrences (all) | 2 | 2 | |
| Sinusitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Oesophageal candidiasis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 2 | |
| Tooth abscess | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 1 / 74 (1.35%) | |
| occurrences (all) | 1 | 1 | |
| Urinary tract infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 6 / 74 (8.11%) | |
| occurrences (all) | 3 | 10 | |

| | | | |
|---|---|---|---|
| Vulvovaginal mycotic infection | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Tracheitis | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 5 / 77 (6.49%) | 6 / 74 (8.11%) | |
| occurrences (all) | 7 | 7 | |
| Hypocalcaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 4 / 74 (5.41%) | |
| occurrences (all) | 3 | 4 | |
| Electrolyte imbalance | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Dehydration | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 2 / 74 (2.70%) | |
| occurrences (all) | 2 | 2 | |
| Decreased appetite | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 16 / 77 (20.78%) | 17 / 74 (22.97%) | |
| occurrences (all) | 17 | 20 | |
| Cachexia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Hyperkalaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hypermagnesaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Hypernatraemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypertriglyceridaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 1 / 74 (1.35%) | |
| occurrences (all) | 7 | 1 | |
| Hyperuricaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 3 / 74 (4.05%) | |
| occurrences (all) | 6 | 4 | |
| Hypoalbuminaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 5 / 77 (6.49%) | 10 / 74 (13.51%) | |
| occurrences (all) | 6 | 16 | |
| Hypercholesterolaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Malnutrition | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 1 / 74 (1.35%) | |
| occurrences (all) | 0 | 1 | |
| Iron deficiency | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|---|
| Hypoproteinaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 2 / 77 (2.60%) | 0 / 74 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Hypophosphataemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 0 / 77 (0.00%) | 5 / 74 (6.76%) | |
| occurrences (all) | 0 | 5 | |
| Hypophagia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 1 / 77 (1.30%) | 0 / 74 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hyponatraemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 9 / 77 (11.69%) | 6 / 74 (8.11%) | |
| occurrences (all) | 15 | 13 | |
| Hypomagnesaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 4 / 74 (5.41%) | |
| occurrences (all) | 3 | 5 | |
| Hypokalaemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 3 / 77 (3.90%) | 4 / 74 (5.41%) | |
| occurrences (all) | 3 | 4 | |
| Hypochloraemia | | | |
| alternative dictionary used: MedDRA 24.0 | | | |
| subjects affected / exposed | 4 / 77 (5.19%) | 1 / 74 (1.35%) | |
| occurrences (all) | 6 | 1 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 05 March 2019 | • To include Programmed death-ligand 1 (PD-L1) expression in tumor cells as stratification factor in the expansion part of the study.<br>• To include information regarding PD-L1 tumor expression and clarify inclusion criteria.<br>• To add details on planned tests for overall survival analyses. |
| 05 July 2019 | • To provide detailed information regarding the Independent Data Monitoring Committee (IDMC) safety reviews.<br>• To add evaluation of a potential biomarker.<br>• To clarify that bone palliative radiotherapy `is allowed during the study.<br>• To exclude participants with history of bleeding diatheses or recent major bleeding events.<br>• To specify the sequence of treatment administration when the radiotherapy is delivered at a separate location. |
| 22 June 2021 | • To reduce the sample size from 350 subjects to approximately 160 subjects to provide an earlier result from the primary analysis to give insight into the potential benefit of M7824 in subjects with unresectable Stage III NSCLC.<br>• To update the risk classification and minimization measures. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported