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 Units: Subjects			
Age Continuous Units: Years			
arithmetic mean	64.7	64.9	
standard deviation	± 9.35	± 8.94	-
Sex: Female, Male Units: subjects			
Female	20	16	36
Male	55	62	117
Race (NIH/OMB) 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) 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			

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

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			

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 alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	4 / 77 (5.19%)	1 / 74 (1.35%)	
occurrences (all)	4	1	
Blood creatine increased 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 alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 77 (2.60%)	4 / 74 (5.41%)	
occurrences (all)	2	8	
Blood creatinine increased alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	3 / 77 (3.90%)	4 / 74 (5.41%)	
occurrences (all)	4	4	
Blood glucose increased 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 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 alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	1 / 77 (1.30%)	1 / 74 (1.35%)	
occurrences (all)	1	1	
Blood triglycerides increased alternative dictionary used: MedDRA 24.0			

subjects affected / exposed	1 / 77 (1.30%)	0 / 74 (0.00%)	
occurrences (all)	1	0	
Blood urea increased 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 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 alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	2 / 77 (2.60%)	1 / 74 (1.35%)	
occurrences (all)	2	2	
Transaminases increased alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 77 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	7 / 77 (9.09%)	5 / 74 (6.76%)	
occurrences (all)	13	7	
Gastric pH decreased 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 alternative dictionary used: MedDRA 24.0			
subjects affected / exposed	0 / 77 (0.00%)	1 / 74 (1.35%)	
occurrences (all)	0	2	
Hepatic enzyme increased 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	

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			

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			

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			

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			

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			

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	

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			

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			

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			

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	

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			

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. • To include information regarding PD-L1 tumor expression and clarify inclusion criteria. • 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. • To add evaluation of a potential biomarker. • To clarify that bone palliative radiotherapy `is allowed during the study. • To exclude participants with history of bleeding diatheses or recent major bleeding events. • 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. • 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