Clinical trial results:
A Phase II, Open-label, Multicentre, International Study of Durvalumab Following Radiation Therapy in Patients with Stage III, Unresectable Non-Small Cell Lung Cancer Who Are Ineligible for Chemotherapy (DUART)

Summary

EudraCT number	2019-004336-31
Trial protocol	FR PL IT
Global end of trial date	25 November 2024

Results information

Result version number	v1 (current)
This version publication date	02 January 2025
First version publication date	02 January 2025

Trial information

Trial identification

Sponsor protocol code	D4194C00009

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04249362
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	AstraZeneca, Södertälje, Sweden, 151 85
Public contact	Global Clinical Lead, AstraZeneca, +1 8772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 8772409479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 December 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 November 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability profile of durvalumab as defined by Grade 3 and Grade 4 possibly related adverse events (PRAEs) within 6 months from the initiation of durvalumab treatment.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Conference on Harmonisation (ICH)/Good Clinical Practice, applicable regulatory requirements and the AstraZeneca policy on Bioethics. The Investigator or his/her representative explained the nature of the study to the subject or his/her legally authorised representative and answered all questions regarding the study. Subjects were informed that their participation was voluntary. Subjects or their legally authorised representative were required to sign a statement of informed consent that met the requirements of 21 CFR 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act (HIPAA) requirements, where applicable, and the Institutional Review Board (IRB)/Independent Ethics Committee (IEC) or

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 November 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Italy: 47
Country: Number of subjects enrolled	Poland: 30
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Spain: 9
Worldwide total number of subjects	102
EEA total number of subjects	97

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)	8
From 65 to 84 years	84
85 years and over	10

Subject disposition

Recruitment

Recruitment details:

Patients were enrolled and received study treatment at 29 sites in 5 countries (France, Italy, Poland, Russian Federation, and Spain). The data in this report are based on study start date (first patient enrolled: 26 November 2020 till final analyses data cut-off date of 06 December 2023.

Pre-assignment

Screening details:

Eligible patients with Stage III unresectable Non-Small Cell Lung Cancer (NSCLC), Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 to 2, treated with radiotherapy and ineligible for chemotherapy, were enrolled. One patient had an important protocol deviation. Study assessments followed the schedule.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Durvalumab Cohort A: Standard radiotherapy (RT)

Arm description:

Patients who received standard RT [60 gray (GY) ± 10% or hypofractionated bioequivalent dose (BED)] before study entry were administered a fixed dose of 1500 mg of durvalumab via intravenous (IV) infusion every 4 weeks (q4w) for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the response evaluation criteria in solid tumors version (RECIST 1.1), unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

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

Dosage and administration details:

Patients were administered a fixed dose of 1500 mg of durvalumab via intravenous (IV) infusion every 4 weeks (q4w)

Arm title	Durvaumab Cohort B: Palliative radiotherapy (RT)

Arm description:

Patients who received palliative RT [40 to < 54 Gy or hypofractionated BED] before study entry were administered a fixed dose of 1500 mg of durvalumab via IV infusion q4w for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the RECIST 1.1, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

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

Dosage and administration details:

Patients were administered a fixed dose of 1500 mg of durvalumab via intravenous (IV) infusion every 4 weeks (q4w)

Number of subjects in period 1	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)
Started	53	49
Completed	53	49

Baseline characteristics

Reporting groups	
Reporting group title	Durvalumab Cohort A: Standard radiotherapy (RT)
Reporting group description:	
Patients who received standard RT [60 gray (GY) ± 10% or hypofractionated bioequivalent dose (BED)] before study entry were administered a fixed dose of 1500 mg of durvalumab via intravenous (IV) infusion every 4 weeks (q4w) for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the response evaluation criteria in solid tumors version (RECIST 1.1), unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.	
Reporting group title	Durvaumab Cohort B: Palliative radiotherapy (RT)
Reporting group description:	
Patients who received palliative RT [40 to < 54 Gy or hypofractionated BED] before study entry were administered a fixed dose of 1500 mg of durvalumab via IV infusion q4w for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the RECIST 1.1, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.	

Reporting group values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Total
Number of subjects	53	49	102
Age categorical Units: Patients			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	6	2	8
From 65-84 years	44	40	84
85 years and over	3	7	10
Age Continuous Units: Years			
arithmetic mean	74.7	78.8	
standard deviation	± 9.18	± 6.71	-
Sex: Female, Male Units: Patients			
Female	15	14	29
Male	38	35	73
Race, Customized Units: Subjects			
White	46	45	91
Other	1	0	1
Unknown	3	1	4
Missing	3	3	6
Ethnicity, Customized Units: Subjects			
Hispanic or Latino	2	3	5

Not Hispanic or Latino	45	43	88
Missing	6	3	9

Subject analysis sets

Subject analysis set title	Durvalumab total
Subject analysis set type	Safety analysis

Subject analysis set description:

Patients who received standard RT [60 gray (GY) ± 10% or hypofractionated BED)] or palliative RT [40 to < 54 Gy or hypofractionated BED] before study entry were administered a fixed dose of 1500 mg of durvalumab via IV infusion q4w for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the RECIST 1.1, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

Subject analysis set title	Durvalumab responders
Subject analysis set type	Safety analysis

Subject analysis set description:

Patients who received standard RT [60 gray (GY) ± 10% or hypofractionated BED)] or palliative RT [40 to < 54 Gy or hypofractionated BED] before study entry were administered a fixed dose of 1500 mg of durvalumab via IV infusion q4w for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the RECIST 1.1, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met. This group includes patients with an overall response of complete response (CR) or partial response (PR) (confirmed by a follow-up scan at least 4 weeks after showing CR or PR) per RECIST 1.1 criteria.

Reporting group values	Durvalumab total	Durvalumab responders	
Number of subjects	102	30	
Age categorical Units: Patients			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	8		
From 65-84 years	84		
85 years and over	10		
Age Continuous Units: Years			
arithmetic mean	76.7		
standard deviation	± 8.32	±	
Sex: Female, Male Units: Patients			
Female	29		
Male	73		
Race, Customized Units: Subjects			
White	91		
Other	1		
Unknown	4		
Missing	6		

Ethnicity, Customized Units: Subjects			
Hispanic or Latino	5		
Not Hispanic or Latino	88		
Missing	9		

End points

End points reporting groups

Reporting group title	Durvalumab Cohort A: Standard radiotherapy (RT)

Reporting group description:

Patients who received standard RT [60 gray (GY) ± 10% or hypofractionated bioequivalent dose (BED)] before study entry were administered a fixed dose of 1500 mg of durvalumab via intravenous (IV) infusion every 4 weeks (q4w) for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the response evaluation criteria in solid tumors version (RECIST 1.1), unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

Reporting group title	Durvaumab Cohort B: Palliative radiotherapy (RT)

Reporting group description:

Patients who received palliative RT [40 to < 54 Gy or hypofractionated BED] before study entry were administered a fixed dose of 1500 mg of durvalumab via IV infusion q4w for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the RECIST 1.1, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

Subject analysis set title	Durvalumab total
Subject analysis set type	Safety analysis

Subject analysis set description:

Patients who received standard RT [60 gray (GY) ± 10% or hypofractionated BED)] or palliative RT [40 to < 54 Gy or hypofractionated BED] before study entry were administered a fixed dose of 1500 mg of durvalumab via IV infusion q4w for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the RECIST 1.1, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

Subject analysis set title	Durvalumab responders
Subject analysis set type	Safety analysis

Subject analysis set description:

Patients who received standard RT [60 gray (GY) ± 10% or hypofractionated BED)] or palliative RT [40 to < 54 Gy or hypofractionated BED] before study entry were administered a fixed dose of 1500 mg of durvalumab via IV infusion q4w for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the RECIST 1.1, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met. This group includes patients with an overall response of complete response (CR) or partial response (PR) (confirmed by a follow-up scan at least 4 weeks after showing CR or PR) per RECIST 1.1 criteria.

Primary: Number of patients with Grade 3 and Grade 4 possibly-related adverse events (PRAEs)

End point title	Number of patients with Grade 3 and Grade 4 possibly-related adverse events (PRAEs)[1]

End point description:

The safety and tolerability profile of durvalumab as defined by Grade 3 and Grade 4 PRAEs within 6 months from the initiation of durvalumab treatment. A PRAE was any TEAE with a possible relatedness to durvalumab, or where the relatedness was missing. If relatedness of a TEAE was missing at the primary DCO (30 March 2023) the TEAE was considered a PRAE. The end point included safety analysis set, consisted of all patients who received at least one dose of durvalumab treatment.

End point type	Primary

End point timeframe:

From first dose of durvalumab treatment until 6 months after initiation of durvalumab treatment

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: No statistical analysis was performed.

End point values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Durvalumab total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	49	102	
Units: Patients	5	5	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Median Progression-free survival (mPFS)

End point title	Median Progression-free survival (mPFS)

End point description:

Progression-free survival is defined as the time from the date of first dose of durvalumab until the date of objective disease progression or death (by any cause in the absence of progression) regardless of whether the patient discontinues durvalumab or receives another anticancer therapy prior to progression according to RECIST 1.1 as assessed by the Investigator. Patients who had not progressed or died at the time of analysis were censored at the date of their last evaluable tumor assessment. If a patient progressed or died after two or more missed visits, they were censored at the date of the latest evaluable assessment prior to the missed visits. The end point included safety analysis set, consisted of all patients who received at least one dose of durvalumab treatment.

End point type	Secondary

End point timeframe:

From the first date of treatment until the date of objective disease progression or death or data cut-off date (36 months)

End point values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Durvalumab total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	49	102	
Units: Months				
median (confidence interval 95%)	10.3 (7.49 to 16.56)	7.6 (5.55 to 11.04)	9.2 (7.39 to 11.93)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival at 6 months (PFS6)

End point title	Progression-free survival at 6 months (PFS6)

End point description:

Progression-free survival is defined as the time from the date of first dose of durvalumab until the date of objective disease progression or death (by any cause in the absence of progression) regardless of

whether the patient discontinues durvalumab or receives another anticancer therapy prior to progression according to RECIST 1.1 as assessed by the Investigator. Patients who had not progressed or died at the time of analysis were censored at the date of their last evaluable tumor assessment. If a patient progressed or died after two or more missed visits, they were censored at the date of the latest evaluable assessment prior to the missed visits. The end point included safety analysis set, consisted of all patients who received at least one dose of durvalumab treatment.

End point type	Secondary

End point timeframe:

From the first date of treatment until the date of objective disease progression or death (6 months)

End point values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Durvalumab total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	49	102	
Units: Percentage of patients				
number (confidence interval 95%)	67.1 (51.96 to 78.43)	59.3 (43.38 to 72.07)	63.3 (52.62 to 72.25)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival at 12 months (PFS12)

End point title	Progression-free survival at 12 months (PFS12)

End point description:

Progression-free survival is defined as the time from the date of first dose of durvalumab until the date of objective disease progression or death (by any cause in the absence of progression) regardless of whether the patient discontinues durvalumab or receives another anticancer therapy prior to progression according to RECIST 1.1 as assessed by the Investigator. Patients who had not progressed or died at the time of analysis were censored at the date of their last evaluable tumor assessment. If a patient progressed or died after two or more missed visits, they were censored at the date of the latest evaluable assessment prior to the missed visits. The end point included safety analysis set, consisted of all patients who received at least one dose of durvalumab treatment.

End point type	Secondary

End point timeframe:

From the first date of treatment until the date of objective disease progression or death (12 months)

End point values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Durvalumab total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	49	102	
Units: Percentage of patients				
number (confidence interval 95%)	46.8 (31.88 to 60.36)	31.8 (18.13 to 46.32)	39.6 (29.28 to 49.76)	

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR)

End point title	Objective response rate (ORR)

End point description:

The ORR is the proportion (%) of patients with an overall response of complete response (CR) or partial response (PR) (confirmed by a follow-up scan at least 4 weeks after showing CR or PR) per RECIST 1.1 criteria. CR is disappearance of all target lesions (TLs) since baseline. Any pathological lymph nodes selected as TLs must have a reduction in short axis diameter to < 10 mm. PR is at least a 30% decrease in the sum of the diameters of TL, taking as reference the baseline sum of diameters. The end point included safety analysis set, consisted of all patients who received at least one dose of durvalumab treatment.

End point type	Secondary

End point timeframe:

From 8 weeks ±1 week after durvalumab treatment initiation and continue every 8 weeks (q8w) ±1 week through 48 weeks and every 12 weeks (q12w) ±1 week until disease progression or data cut-off (36 months)

End point values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Durvalumab total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	49	102	
Units: Percentage of patients				
number (confidence interval 95%)	34.0 (21.5 to 48.3)	24.5 (13.3 to 38.9)	29.4 (20.8 to 39.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival at 12 months (OS12)

End point title	Overall survival at 12 months (OS12)

End point description:

The OS is defined as the time from the date of first dose of durvalumab until death due to any cause. Patients who were not known to have died at the time of analysis were censored at the last recorded date when they were known to have been alive. The end point included safety analysis set, consisted of all patients who received at least one dose of durvalumab treatment.

End point type	Secondary

End point timeframe:

From the first date of treatment until death due to any cause (12 months)

End point values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Durvalumab total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	49	102	
Units: Percentage of patients				
number (confidence interval 95%)	64.0 (49.01 to 75.58)	65.5 (49.87 to 77.26)	64.7 (54.21 to 73.34)	

Statistical analyses

No statistical analyses for this end point

Secondary: Median overall survival (mOS)

End point title	Median overall survival (mOS)

End point description:

The OS is defined as the time from the date of first dose of durvalumab until death due to any cause. Patients who were not known to have died at the time of analysis were censored at the last recorded date when they were known to have been alive. Here, arbitrary value 9999.9999 represents data that were not calculable due to insufficient number of patients with events. The end point included safety analysis set, consisted of all patients who received at least one dose of durvalumab treatment.

End point type	Secondary

End point timeframe:

From the first date of treatment until death or data cut-off due to any cause (36 months)

End point values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Durvalumab total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	49	102	
Units: Months				
median (confidence interval 95%)	21.1 (11.60 to 9999.9999)	16.8 (10.64 to 9999.9999)	21.1 (14.75 to 9999.9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DoR)

End point title	Duration of response (DoR)

End point description:

The DoR is defined as the time from the date of first documented response (which is subsequently confirmed) until the first date of documented progression per RECIST1.1 or death in the absence of disease progression. The arbitary value 9999.9999 represents data that data were not calculable due to insufficient number of patients with events. The end point included safety analysis set, consisted of all patients who received at least one dose of durvalumab treatment.

End point type	Secondary

End point timeframe:

From 8 weeks ±1 week after durvalumab treatment initiation and continue every 8 weeks (q8w) ±1 week through 48 weeks and every 12 weeks (q12w) ±1 week until disease progression or data cut-off (36 months)

End point values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Durvalumab responders	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	18	12	30	
Units: Weeks				
median (confidence interval 95%)	56.9 (31.00 to 9999.9999)	34.1 (24.29 to 9999.9999)	56.9 (31.14 to 9999.9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Lung cancer mortality

End point title	Lung cancer mortality

End point description:

The lung cancer mortality (NSCLC-related death) is assessed using the deaths which are reported as 'NSCLC-related' and is defined as the time (days) from the date of first dose of durvalumab until date of death due to lung cancer. The arbitary value 9999.9999 represents data that data were not calculable due to insufficient number of patients with events. The endpoint included safety analysis set, consisted of all patients who received at least one dose of durvalumab treatment.

End point type	Secondary

End point timeframe:

From date of treatment start until death due to lung cancer (36 months)

End point values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Durvalumab total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	49	102	
Units: Months				

median (confidence interval 95%)	30.9 (16.92 to 9999.9999)	9999.9999 (14.75 to 9999.9999)	30.9 (16.82 to 9999.9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with events (AEs)

End point title	Number of patients with events (AEs)

End point description:

The safety and tolerability profile of durvalumab treatment, including all adverse events (AEs) was assessed. The end point included safety analysis set, consisted of all patients who received at least one dose of durvalumab treatment. Common Terminology Criteria for Adverse Events-CTCAE; possibly related to durvalumab treatment-PRTT; discontinuation of treatment- DT; treatment interruption- TI; including- incl. and adverse event of potential interest-AEPI.

End point type	Secondary

End point timeframe:

From screening (Day -28) till data cut-off (36 months)

End point values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Durvalumab total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	49	102	
Units: Patients				
Any AE	50	49	99	
Any PRAE (Investigator-assessed [IA])	31	31	62	
Any AE of CTCAE Grade (Gr) 3 or Gr 4	20	21	41	
Any AE of CTCAE Gr 3 or Gr 4, PRTT (IA)	6	5	11	
Any AE resulted in death	5	2	7	
Any AE resulted death, PRTT (IA)	1	0	1	
Any SAE incl. events resulted in death	23	18	41	
Any SAE incl. events resulted in death, PRTT (IA)	5	3	8	
Any AE leading to DT	13	9	22	
Any AE leading to DT, PRTT (IA)	7	5	12	
Any AE leading to TI	25	23	48	
Any AE leading to TI, PRTT	6	7	13	
Any AESI incl. events resulted in death (IA)	25	21	46	
Any AESI incl. events resulted in death, PRTT (IA)	19	14	33	
Any AEPI incl. events resulted in death (IA)	21	22	43	
Any AEPI incl. events resulted in death, PRTT (IA)	14	15	29	

Any imAE (IA)	27	24	51	
Any imAE, PRTT (IA)	26	24	50	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with adverse events of special interests (AESIs)

End point title	Number of patients with adverse events of special interests (AESIs)

End point description:

The safety and tolerability profile of durvalumab treatment, including all adverse events (AEs) was assessed. An AESI is an AE of scientific and medical interest specific to the understanding of durvalumab. AESIs for durvalumab include, but are not limited to, events with a potential inflammatory or immune-mediated mechanism and which may require more frequent monitoring and/or interventions such as steroids, immunosuppressants and/or hormone replacement therapy. Here, number of patients experienced AESIs are presented. Serious adverse event of special interests (SAESIs). The end point included safety analysis set, consisted of all patients who received at least one dose of durvalumab treatment. Common Terminology Criteria for Adverse Events-CTCAE; discontinuation of treatment- DT; including- incl. and causally related to treatment- CRT.

End point type	Secondary

End point timeframe:

From screening (Day -28) till data cut-off (36 months)

End point values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Durvalumab total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	49	102	
Units: Patients				
Any AESIs	25	21	46	
Any AESIs of CTCAE Gr 3 or 4	4	1	5	
Any SAESIs incl. events resulted in death	4	1	5	
Any AESIs resulted in death	1	0	1	
Any AESIs, CRT	19	14	33	
Any AESIs of CTCAE Gr 3 or 4, CRT	4	1	5	
Any SAESIs, CRT	4	1	5	
Any AESIs resulted in death, CRT	1	0	1	
AESIs: Received systemic corticosteroids	5	8	13	
AESIs: Received high dose steroids	4	6	10	
AESIs: Received endocrine therapy	6	5	11	
AESIs: Received other immunosuppressants	0	0	0	
Any AESIs leading to DT	4	3	7	
AESIs: Event outcome resolved	13	12	25	
AESIs: Event outcome not resolved	11	9	20	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of patients with immune-mediated adverse events (imAEs)

End point title	Number of patients with immune-mediated adverse events (imAEs)

End point description:

The safety and tolerability profile of durvalumab treatment, including all adverse events (AEs) was assessed. An imAE is defined as an AESI that is associated with drug exposure and is consistent with an immune-mediated mechanism of action and where there is no clear alternate etiology. Here, number of patients experienced imAEs are presented. Immune-mediated serious adverse events (imSAEs). The end point included safety analysis set, consisted of all patients who received at least one dose of durvalumab treatment. Common Terminology Criteria for Adverse Events-CTCAE; discontinuation of treatment- DT; including- incl. and causally related to treatment- CRT.

End point type	Secondary

End point timeframe:

From screening (Day -28) till data cut-off (36 months)

End point values	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvaumab Cohort B: Palliative radiotherapy (RT)	Durvalumab total	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	53	49	102	
Units: Patients				
Any imAEs	11	15	26	
Any imAEs of CTCAE Gr 3 or 4	2	3	5	
Any imSAEs incl. events resulted in death	3	2	5	
Any imAEs resulted in death	1	0	1	
Any imAEs, CRT	10	12	22	
Any imAEs of CTCAE Gr 3 or 4, CRT	2	3	5	
Any imSAEs, CRT	3	2	5	
Any imAEs resulted in death, CRT	1	0	1	
imAEs: Received systemic corticosteroids	7	13	20	
imAEs: Received high dose steroids	5	7	12	
imAEs: Received endocrine therapy	6	5	11	
imAEs: Received other immunosuppressants	0	0	0	
Any imAEs leading to DT	3	4	7	
imAEs: Event outcome resolved	5	8	13	
imAEs: Event outcome not resolved	5	7	12	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening (Day -28) till data cut-off (36 months)

Adverse event reporting additional description:

Frequency threshold for reporting non-serious adverse events is 2.5. However, due to tool limitation in the below field 2 has been entered.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Durvalumab Cohort A: Standard radiotherapy (RT)

Reporting group description:

Patients who received standard RT [60 gray (GY) ± 10% or hypofractionated bioequivalent dose (BED)] before study entry were administered a fixed dose of 1500 mg of durvalumab via intravenous (IV) infusion every 4 weeks (q4w) for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the response evaluation criteria in solid tumors version (RECIST 1.1), unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

Reporting group title	Durvalumab total

Reporting group description:

Patients who received standard RT [60 gray (GY) ± 10% or hypofractionated BED)] or palliative RT [40 to < 54 Gy or hypofractionated BED] before study entry were administered a fixed dose of 1500 mg of durvalumab via IV infusion q4w for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the RECIST 1.1, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

Reporting group title	Durvaumab Cohort B: Palliative radiotherapy (RT)

Reporting group description:

Patients who received palliative RT [40 to < 54 Gy or hypofractionated BED] before study entry were administered a fixed dose of 1500 mg of durvalumab via IV infusion q4w for a duration of 12 months (up to 13 doses/cycles), or until clinical progression or radiological progression defined by the RECIST 1.1, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

Serious adverse events	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvalumab total	Durvaumab Cohort B: Palliative radiotherapy (RT)
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 53 (43.40%)	41 / 102 (40.20%)	18 / 49 (36.73%)
number of deaths (all causes)	23	46	23
number of deaths resulting from adverse events	5	7	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Transitional cell carcinoma			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circulatory collapse			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 53 (1.89%)	2 / 102 (1.96%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 1
Asthenia			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	1 / 1	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 53 (1.89%)	2 / 102 (1.96%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 53 (1.89%)	2 / 102 (1.96%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			

subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Subdural haemorrhage			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocarditis			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular failure			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 53 (1.89%)	5 / 102 (4.90%)	4 / 49 (8.16%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Atrial fibrillation			

subjects affected / exposed	2 / 53 (3.77%)	2 / 102 (1.96%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatomyositis			

subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Immune-mediated nephritis			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter sepsis			
subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			

subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 53 (0.00%)	1 / 102 (0.98%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 53 (5.66%)	5 / 102 (4.90%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	1 / 3	1 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 53 (1.89%)	1 / 102 (0.98%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Durvalumab Cohort A: Standard radiotherapy (RT)	Durvalumab total	Durvaumab Cohort B: Palliative radiotherapy (RT)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 53 (88.68%)	92 / 102 (90.20%)	45 / 49 (91.84%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 53 (0.00%)	5 / 102 (4.90%)	5 / 49 (10.20%)
occurrences (all)	0	5	5
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	13 / 53 (24.53%)	21 / 102 (20.59%)	8 / 49 (16.33%)
occurrences (all)	14	23	9
Fatigue			
subjects affected / exposed	1 / 53 (1.89%)	11 / 102 (10.78%)	10 / 49 (20.41%)
occurrences (all)	1	11	10
Oedema peripheral			

subjects affected / exposed	3 / 53 (5.66%)	8 / 102 (7.84%)	5 / 49 (10.20%)
occurrences (all)	3	8	5
Pyrexia			
subjects affected / exposed	8 / 53 (15.09%)	16 / 102 (15.69%)	8 / 49 (16.33%)
occurrences (all)	9	18	9
Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	3 / 53 (5.66%)	6 / 102 (5.88%)	3 / 49 (6.12%)
occurrences (all)	3	6	3
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 53 (3.77%)	6 / 102 (5.88%)	4 / 49 (8.16%)
occurrences (all)	2	6	4
Cough			
subjects affected / exposed	9 / 53 (16.98%)	21 / 102 (20.59%)	12 / 49 (24.49%)
occurrences (all)	13	26	13
Dyspnoea			
subjects affected / exposed	11 / 53 (20.75%)	19 / 102 (18.63%)	8 / 49 (16.33%)
occurrences (all)	11	19	8
Haemoptysis			
subjects affected / exposed	2 / 53 (3.77%)	5 / 102 (4.90%)	3 / 49 (6.12%)
occurrences (all)	2	5	3
Pneumonitis			
subjects affected / exposed	3 / 53 (5.66%)	7 / 102 (6.86%)	4 / 49 (8.16%)
occurrences (all)	3	7	4
Pulmonary fibrosis			
subjects affected / exposed	2 / 53 (3.77%)	2 / 102 (1.96%)	0 / 49 (0.00%)
occurrences (all)	2	2	0
Respiratory failure			
subjects affected / exposed	2 / 53 (3.77%)	2 / 102 (1.96%)	0 / 49 (0.00%)
occurrences (all)	2	2	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 53 (0.00%)	2 / 102 (1.96%)	2 / 49 (4.08%)
occurrences (all)	0	2	2
Investigations			

Weight decreased			
subjects affected / exposed	2 / 53 (3.77%)	2 / 102 (1.96%)	0 / 49 (0.00%)
occurrences (all)	2	2	0
Neutrophil count increased			
subjects affected / exposed	4 / 53 (7.55%)	4 / 102 (3.92%)	0 / 49 (0.00%)
occurrences (all)	6	6	0
Lipase increased			
subjects affected / exposed	1 / 53 (1.89%)	3 / 102 (2.94%)	2 / 49 (4.08%)
occurrences (all)	2	4	2
Alanine aminotransferase increased			
subjects affected / exposed	4 / 53 (7.55%)	7 / 102 (6.86%)	3 / 49 (6.12%)
occurrences (all)	4	7	3
Amylase increased			
subjects affected / exposed	3 / 53 (5.66%)	5 / 102 (4.90%)	2 / 49 (4.08%)
occurrences (all)	3	7	4
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 53 (5.66%)	4 / 102 (3.92%)	1 / 49 (2.04%)
occurrences (all)	4	5	1
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 53 (5.66%)	5 / 102 (4.90%)	2 / 49 (4.08%)
occurrences (all)	3	6	3
Blood creatinine increased			
subjects affected / exposed	2 / 53 (3.77%)	6 / 102 (5.88%)	4 / 49 (8.16%)
occurrences (all)	2	8	6
Blood lactate dehydrogenase increased			
subjects affected / exposed	3 / 53 (5.66%)	4 / 102 (3.92%)	1 / 49 (2.04%)
occurrences (all)	3	4	1
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	2 / 53 (3.77%)	2 / 102 (1.96%)	0 / 49 (0.00%)
occurrences (all)	3	3	0
Blood urea increased			
subjects affected / exposed	3 / 53 (5.66%)	4 / 102 (3.92%)	1 / 49 (2.04%)
occurrences (all)	5	6	1
Blood uric acid increased			

subjects affected / exposed	2 / 53 (3.77%)	3 / 102 (2.94%)	1 / 49 (2.04%)
occurrences (all)	2	3	1
C-reactive protein increased			
subjects affected / exposed	4 / 53 (7.55%)	5 / 102 (4.90%)	1 / 49 (2.04%)
occurrences (all)	4	5	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 53 (5.66%)	5 / 102 (4.90%)	2 / 49 (4.08%)
occurrences (all)	3	5	2
Injury, poisoning and procedural complications			
Radiation pneumonitis			
subjects affected / exposed	1 / 53 (1.89%)	3 / 102 (2.94%)	2 / 49 (4.08%)
occurrences (all)	1	3	2
Spinal compression fracture			
subjects affected / exposed	0 / 53 (0.00%)	2 / 102 (1.96%)	2 / 49 (4.08%)
occurrences (all)	0	2	2
Fall			
subjects affected / exposed	0 / 53 (0.00%)	2 / 102 (1.96%)	2 / 49 (4.08%)
occurrences (all)	0	2	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 53 (3.77%)	3 / 102 (2.94%)	1 / 49 (2.04%)
occurrences (all)	2	3	1
Headache			
subjects affected / exposed	1 / 53 (1.89%)	3 / 102 (2.94%)	2 / 49 (4.08%)
occurrences (all)	1	3	2
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	2 / 53 (3.77%)	2 / 102 (1.96%)	0 / 49 (0.00%)
occurrences (all)	3	3	0
Thrombocytosis			
subjects affected / exposed	2 / 53 (3.77%)	2 / 102 (1.96%)	0 / 49 (0.00%)
occurrences (all)	2	2	0
Lymphopenia			
subjects affected / exposed	2 / 53 (3.77%)	4 / 102 (3.92%)	2 / 49 (4.08%)
occurrences (all)	2	4	2
Leukocytosis			

subjects affected / exposed	3 / 53 (5.66%)	5 / 102 (4.90%)	2 / 49 (4.08%)
occurrences (all)	3	5	2
Anaemia			
subjects affected / exposed	13 / 53 (24.53%)	19 / 102 (18.63%)	6 / 49 (12.24%)
occurrences (all)	14	22	8
Eye disorders			
Periorbital oedema			
subjects affected / exposed	0 / 53 (0.00%)	2 / 102 (1.96%)	2 / 49 (4.08%)
occurrences (all)	0	2	2
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 53 (1.89%)	3 / 102 (2.94%)	2 / 49 (4.08%)
occurrences (all)	1	3	2
Constipation			
subjects affected / exposed	3 / 53 (5.66%)	13 / 102 (12.75%)	10 / 49 (20.41%)
occurrences (all)	3	15	12
Diarrhoea			
subjects affected / exposed	3 / 53 (5.66%)	7 / 102 (6.86%)	4 / 49 (8.16%)
occurrences (all)	3	8	5
Nausea			
subjects affected / exposed	0 / 53 (0.00%)	4 / 102 (3.92%)	4 / 49 (8.16%)
occurrences (all)	0	4	4
Stomatitis			
subjects affected / exposed	1 / 53 (1.89%)	3 / 102 (2.94%)	2 / 49 (4.08%)
occurrences (all)	1	3	2
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	0 / 53 (0.00%)	2 / 102 (1.96%)	2 / 49 (4.08%)
occurrences (all)	0	2	2
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	2 / 53 (3.77%)	2 / 102 (1.96%)	0 / 49 (0.00%)
occurrences (all)	2	2	0
Erythema			
subjects affected / exposed	0 / 53 (0.00%)	2 / 102 (1.96%)	2 / 49 (4.08%)
occurrences (all)	0	2	2
Pruritus			

subjects affected / exposed	5 / 53 (9.43%)	13 / 102 (12.75%)	8 / 49 (16.33%)
occurrences (all)	5	14	9
Rash			
subjects affected / exposed	2 / 53 (3.77%)	3 / 102 (2.94%)	1 / 49 (2.04%)
occurrences (all)	2	3	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 53 (3.77%)	3 / 102 (2.94%)	1 / 49 (2.04%)
occurrences (all)	2	3	1
Urinary incontinence			
subjects affected / exposed	0 / 53 (0.00%)	2 / 102 (1.96%)	2 / 49 (4.08%)
occurrences (all)	0	2	2
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	6 / 53 (11.32%)	11 / 102 (10.78%)	5 / 49 (10.20%)
occurrences (all)	6	11	5
Hypothyroidism			
subjects affected / exposed	9 / 53 (16.98%)	15 / 102 (14.71%)	6 / 49 (12.24%)
occurrences (all)	9	17	8
Thyroiditis			
subjects affected / exposed	2 / 53 (3.77%)	2 / 102 (1.96%)	0 / 49 (0.00%)
occurrences (all)	2	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 53 (15.09%)	14 / 102 (13.73%)	6 / 49 (12.24%)
occurrences (all)	10	16	6
Back pain			
subjects affected / exposed	5 / 53 (9.43%)	10 / 102 (9.80%)	5 / 49 (10.20%)
occurrences (all)	5	11	6
Musculoskeletal pain			
subjects affected / exposed	1 / 53 (1.89%)	3 / 102 (2.94%)	2 / 49 (4.08%)
occurrences (all)	1	3	2
Neck pain			
subjects affected / exposed	1 / 53 (1.89%)	3 / 102 (2.94%)	2 / 49 (4.08%)
occurrences (all)	1	3	2
Pain in extremity			

subjects affected / exposed	1 / 53 (1.89%)	3 / 102 (2.94%)	2 / 49 (4.08%)
occurrences (all)	1	3	2
Spinal pain			
subjects affected / exposed	0 / 53 (0.00%)	2 / 102 (1.96%)	2 / 49 (4.08%)
occurrences (all)	0	2	2
Musculoskeletal chest pain			
subjects affected / exposed	0 / 53 (0.00%)	2 / 102 (1.96%)	2 / 49 (4.08%)
occurrences (all)	0	2	2
Infections and infestations			
Pneumonia			
subjects affected / exposed	3 / 53 (5.66%)	6 / 102 (5.88%)	3 / 49 (6.12%)
occurrences (all)	3	7	4
Herpes zoster			
subjects affected / exposed	2 / 53 (3.77%)	2 / 102 (1.96%)	0 / 49 (0.00%)
occurrences (all)	2	2	0
COVID-19			
subjects affected / exposed	6 / 53 (11.32%)	9 / 102 (8.82%)	3 / 49 (6.12%)
occurrences (all)	6	9	3
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 53 (15.09%)	14 / 102 (13.73%)	6 / 49 (12.24%)
occurrences (all)	8	15	7
Hyperkalaemia			
subjects affected / exposed	2 / 53 (3.77%)	6 / 102 (5.88%)	4 / 49 (8.16%)
occurrences (all)	2	9	7

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 August 2023	Amendment 1: Section 4.1, Table 2, Section 7.1.1, Section 7.1.2: the minimum expected safety follow-up period of 90 days following the last dose of durvalumab for patients treated with the study treatment has been detailed and clarified, and accordingly new sections (Section 7.1.1 and 7.1.2) were added. Section 4.4 and Section 6.1.3: a new section as "Continued access to study treatment" was added. Section 9.5: details related to data analysis (DCO for the primary analysis) were added. Section 6: updated the definition for "study treatments" and details of durvalumab in Table 5. Also updated text describing administration of study treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported