Clinical trial results:
A Phase III, Randomized, Multicenter, Double-blind, Placebo-controlled Study to Determine the Efficacy of Adjuvant Durvalumab in Combination with Platinum-based Chemotherapy in Completely Resected Stage II-III NSCLC (MERMAID-1)

Summary

EudraCT number	2020-000556-35
Trial protocol	GB NL DK BG HU DE BE SE PL CZ GR IT FR RO
Global end of trial date	31 August 2023

Results information

Result version number	v1 (current)
This version publication date	08 September 2024
First version publication date	08 September 2024

Trial information

Trial identification

Sponsor protocol code	D910LC00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04385368
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Forskargatan 18, Södertälje, Sweden, 151 85
Public contact	Global Clinical Lead, AstraZeneca AB, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca AB, +1 877-240-9479, 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	31 August 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of durvalumab + standard of care (SoC) chemotherapy compared to placebo + SoC chemotherapy as measured by disease-free survival (DFS) in all participants.

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the following: consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines, applicable International Council for Harmonization Good Clinical Practice Guidelines, and applicable laws and regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 July 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 1
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Brazil: 3
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Greece: 5
Country: Number of subjects enrolled	Hungary: 6
Country: Number of subjects enrolled	India: 3
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Japan: 14
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Korea, Republic of: 3
Country: Number of subjects enrolled	Spain: 2

Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Taiwan: 4
Country: Number of subjects enrolled	Thailand: 2
Country: Number of subjects enrolled	Türkiye: 4
Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Viet Nam: 1
Worldwide total number of subjects	89
EEA total number of subjects	36

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)	43
From 65 to 84 years	46
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase III, multicenter, randomized, double-blind, placebo-controlled study was conducted in participants with completely resected stage II to III non-small cell lung cancer (NSCLC) at 63 sites across 25 countries from 17 July 2020 to 31 August 2023.

Pre-assignment

Screening details:

A total of 89 participants were randomized in a 1:1 ratio to durvalumab given concurrently with SoC chemotherapy followed by durvalumab monotherapy, or to a matched placebo given concurrently with SoC chemotherapy followed by placebo.

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, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Durvalumab + SoC

Arm description:

Participants received durvalumab 1500 milligrams (mg) via intravenous (IV) infusion in combination with SoC chemotherapy on Day 1 of each 3-week cycle for up to 4 cycles, followed by durvalumab monotherapy continued on Day 1 of each 4-week cycle for up to 10 additional cycles until unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.
For participants with tumors of squamous histology, permitted SoC chemotherapy was a combination of carboplatin (area under the serum drug concentration-time curve [AUC] 6) and paclitaxel 200 milligram per square meter (mg/m^2) via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.
For participants with tumors of non-squamous tumor histology, permitted SoC chemotherapy regimens were pemetrexed 500 mg/m^2 in combination with either cisplatin 75 mg/m^2 or carboplatin AUC 5, all via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.

Arm type	Experimental
Investigational medicinal product name	Durvalumab
Investigational medicinal product code	MEDI4736
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Durvalumab was provided as 500-mg vial solution for infusion after dilution, 50 milligrams per milliliter (mg/mL). Participants received durvalumab 1500 mg via IV infusion over 60 minutes on Day 1 of each 3-week cycle for 14 cycles, unless protocol-specified discontinuation criterion was met.

Investigational medicinal product name	Pemetrexed + Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pemetrexed (500 mg/m^2) and carboplatin (AUC 5) on Day 1 of each 3-week cycle for 4 cycles.

Investigational medicinal product name	Pemetrexed + Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion

Routes of administration	Intravenous use

Dosage and administration details:

Pemetrexed (500 mg/m^2) and cisplatin (75 mg/m^2) on Day 1 of each 3-week cycle for 4 cycles.

Investigational medicinal product name	Carboplatin + Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel (200 mg/m^2) and carboplatin (AUC 6) on Day 1 of each 3-week cycle for 4 cycles.

Arm title	Placebo + SoC

Arm description:

Participants received matching placebo via IV infusion in combination with SoC chemotherapy on Day 1 of each 3-week cycle for up to 4 cycles, followed by matching placebo continued on Day 1 of each 4-week cycle for up to 10 additional cycles until unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.
For participants with tumors of squamous histology, permitted SoC chemotherapy was a combination of carboplatin (AUC 6) and paclitaxel 200 mg/m^2 via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.
For participants with tumors of non-squamous tumor histology, permitted SoC chemotherapy regimens were pemetrexed 500 mg/m^2 in combination with either cisplatin 75 mg/m^2 or carboplatin AUC 5, all via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.

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

Dosage and administration details:

Matching placebo was provided as vial solution for infusion after dilution. Participants received matching placebo via IV infusion over 60 minutes on Day 1 of each 3-week cycle for 14 cycles, unless protocol-specified discontinuation criterion was met.

Investigational medicinal product name	Carboplatin + Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel (200 mg/m^2) and carboplatin (AUC 6) on Day 1 of each 3-week cycle for 4 cycles.

Investigational medicinal product name	Pemetrexed + Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pemetrexed (500 mg/m^2) and cisplatin (75 mg/m^2) on Day 1 of each 3-week cycle for 4 cycles.

Investigational medicinal product name	Pemetrexed + Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pemetrexed (500 mg/m^2) and carboplatin (AUC 5) on Day 1 of each 3-week cycle for 4 cycles.

Number of subjects in period 1	Durvalumab + SoC	Placebo + SoC
Started	45	44
Completed	33	36
Not completed	12	8
Physician decision	3	-
Consent withdrawn by subject	4	3
Death	5	5

Baseline characteristics

Reporting groups	
Reporting group title	Durvalumab + SoC

Reporting group description:

Participants received durvalumab 1500 milligrams (mg) via intravenous (IV) infusion in combination with SoC chemotherapy on Day 1 of each 3-week cycle for up to 4 cycles, followed by durvalumab monotherapy continued on Day 1 of each 4-week cycle for up to 10 additional cycles until unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.
For participants with tumors of squamous histology, permitted SoC chemotherapy was a combination of carboplatin (area under the serum drug concentration-time curve [AUC] 6) and paclitaxel 200 milligram per square meter (mg/m^2) via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.
For participants with tumors of non-squamous tumor histology, permitted SoC chemotherapy regimens were pemetrexed 500 mg/m^2 in combination with either cisplatin 75 mg/m^2 or carboplatin AUC 5, all via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.

Reporting group title	Placebo + SoC

Reporting group description:

Participants received matching placebo via IV infusion in combination with SoC chemotherapy on Day 1 of each 3-week cycle for up to 4 cycles, followed by matching placebo continued on Day 1 of each 4-week cycle for up to 10 additional cycles until unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.
For participants with tumors of squamous histology, permitted SoC chemotherapy was a combination of carboplatin (AUC 6) and paclitaxel 200 mg/m^2 via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.
For participants with tumors of non-squamous tumor histology, permitted SoC chemotherapy regimens were pemetrexed 500 mg/m^2 in combination with either cisplatin 75 mg/m^2 or carboplatin AUC 5, all via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.

Reporting group values	Durvalumab + SoC	Placebo + SoC	Total
Number of subjects	45	44	89
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	65.5	64.5	
standard deviation	± 8.78	± 7.37	-
Sex: Female, Male Units: participants			
Female	17	15	32
Male	28	29	57
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	9	18	27
White	35	22	57
Not reported	1	3	4
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	4	1	5
Not Hispanic or Latino	40	43	83
Missing	1	0	1

Subject analysis sets

Subject analysis set title	Durvalumab + SoC: MRD+ Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received durvalumab 1500 mg via IV infusion in combination with SoC chemotherapy on Day 1 of each 3-week cycle for up to 4 cycles, followed by durvalumab monotherapy continued on Day 1 of each 4-week cycle for up to 10 additional cycles until unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.
For participants with tumors of squamous histology, permitted SoC chemotherapy was a combination of carboplatin (AUC 6) and paclitaxel 200 mg/m^2 via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.
For participants with tumors of non-squamous tumor histology, permitted SoC chemotherapy regimens were pemetrexed 500 mg/m^2 in combination with either cisplatin 75 mg/m^2 or carboplatin AUC 5, all via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.

Subject analysis set title	Placebo + SoC: MRD+ Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received matching placebo via IV infusion in combination with SoC chemotherapy on Day 1 of each 3-week cycle for up to 4 cycles, followed by matching placebo continued on Day 1 of each 4-week cycle for up to 10 additional cycles until unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.
For participants with tumors of squamous histology, permitted SoC chemotherapy was a combination of carboplatin (AUC 6) and paclitaxel 200 mg/m^2 via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.
For participants with tumors of non-squamous tumor histology, permitted SoC chemotherapy regimens were pemetrexed 500 mg/m^2 in combination with either cisplatin 75 mg/m^2 or carboplatin AUC 5, all via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.

Reporting group values	Durvalumab + SoC: MRD+ Analysis Set	Placebo + SoC: MRD+ Analysis Set	
Number of subjects	12	11	
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	69.3	67.4	
standard deviation	± 7.41	± 6.22	
Sex: Female, Male			
Units: participants			
Female	6	3	
Male	6	8	
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	2	4	
White	10	7	
Not reported	0	0	
Race/Ethnicity, Customized			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	12	11	
Missing	0	0	

End points

End points reporting groups

Reporting group title	Durvalumab + SoC

Reporting group description:

Participants received durvalumab 1500 milligrams (mg) via intravenous (IV) infusion in combination with SoC chemotherapy on Day 1 of each 3-week cycle for up to 4 cycles, followed by durvalumab monotherapy continued on Day 1 of each 4-week cycle for up to 10 additional cycles until unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.
For participants with tumors of squamous histology, permitted SoC chemotherapy was a combination of carboplatin (area under the serum drug concentration-time curve [AUC] 6) and paclitaxel 200 milligram per square meter (mg/m^2) via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.
For participants with tumors of non-squamous tumor histology, permitted SoC chemotherapy regimens were pemetrexed 500 mg/m^2 in combination with either cisplatin 75 mg/m^2 or carboplatin AUC 5, all via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.

Reporting group title	Placebo + SoC

Reporting group description:

Participants received matching placebo via IV infusion in combination with SoC chemotherapy on Day 1 of each 3-week cycle for up to 4 cycles, followed by matching placebo continued on Day 1 of each 4-week cycle for up to 10 additional cycles until unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.
For participants with tumors of squamous histology, permitted SoC chemotherapy was a combination of carboplatin (AUC 6) and paclitaxel 200 mg/m^2 via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.
For participants with tumors of non-squamous tumor histology, permitted SoC chemotherapy regimens were pemetrexed 500 mg/m^2 in combination with either cisplatin 75 mg/m^2 or carboplatin AUC 5, all via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.

Subject analysis set title	Durvalumab + SoC: MRD+ Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received durvalumab 1500 mg via IV infusion in combination with SoC chemotherapy on Day 1 of each 3-week cycle for up to 4 cycles, followed by durvalumab monotherapy continued on Day 1 of each 4-week cycle for up to 10 additional cycles until unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.
For participants with tumors of squamous histology, permitted SoC chemotherapy was a combination of carboplatin (AUC 6) and paclitaxel 200 mg/m^2 via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.
For participants with tumors of non-squamous tumor histology, permitted SoC chemotherapy regimens were pemetrexed 500 mg/m^2 in combination with either cisplatin 75 mg/m^2 or carboplatin AUC 5, all via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.

Subject analysis set title	Placebo + SoC: MRD+ Analysis Set
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received matching placebo via IV infusion in combination with SoC chemotherapy on Day 1 of each 3-week cycle for up to 4 cycles, followed by matching placebo continued on Day 1 of each 4-week cycle for up to 10 additional cycles until unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.
For participants with tumors of squamous histology, permitted SoC chemotherapy was a combination of carboplatin (AUC 6) and paclitaxel 200 mg/m^2 via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.
For participants with tumors of non-squamous tumor histology, permitted SoC chemotherapy regimens were pemetrexed 500 mg/m^2 in combination with either cisplatin 75 mg/m^2 or carboplatin AUC 5, all via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.

Primary: Disease-free Survival (DFS) in Full Analysis Set (FAS) (Using Investigator Assessments According to Response Evaluation Criteria in Solid Tumors 1.1 [RECIST 1.1])

End point title	Disease-free Survival (DFS) in Full Analysis Set (FAS) (Using Investigator Assessments According to Response Evaluation Criteria in Solid Tumors 1.1 [RECIST 1.1])[1]

End point description:

DFS was defined as the time from the date of randomization until either of the following events, whichever occurred first: disease recurrence using Investigator RECIST 1.1 assessments (i.e., local or regional recurrence, distant recurrence, second primary NSCLC) or death from any cause. The FAS included all randomized participants. 9999 indicates that median and upper limit of confidence interval were not estimable due to insufficient number of participants with events at study closure and due to limited duration of follow-up.

End point type	Primary

End point timeframe:

Every 12 weeks (q12w) ± 1 week until appearance of RECIST 1.1-defined disease recurrence or until primary DFS analysis, up to 33.28 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: As the endpoint was descriptive in nature, no statistical analysis was reported.

End point values	Durvalumab + SoC	Placebo + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	44		
Units: months				
median (confidence interval 95%)	9999 (14.062 to 9999)	9999 (21.914 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: DFS in Minimal Residual Disease-positive (MRD+) Analysis Set (Using Investigator Assessments According to RECIST 1.1)

End point title	DFS in Minimal Residual Disease-positive (MRD+) Analysis Set (Using Investigator Assessments According to RECIST 1.1)

End point description:

DFS was defined as the time from the date of randomization until either of the following events, whichever occurred first: disease recurrence using Investigator RECIST 1.1 assessments (i.e., local or regional recurrence, distant recurrence, second primary NSCLC) or death from any cause. The MRD+ analysis set included all participants in the FAS who were MRD+, as determined by results from the post-surgical plasma sample based on the assay that was used at the time of randomization assay. 9999 indicates that median and/or upper limit of confidence interval were not estimable due to insufficient number of participants with events at study closure and due to limited duration of follow-up.

End point type	Secondary

End point timeframe:

Every 12 weeks (q12w) ± 1 week until appearance of RECIST 1.1-defined disease recurrence or until primary DFS analysis, up to 33.28 months

End point values	Durvalumab + SoC: MRD+ Analysis Set	Placebo + SoC: MRD+ Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	11		
Units: months				
median (confidence interval 95%)	16.7 (2.661 to	9999 (5.585 to		

9999)	9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in FAS

End point title	Overall Survival (OS) in FAS

End point description:

OS was defined as the time from the date of randomization until death due to any cause. Any participant not known to have died at the time of analysis was censored based on the last recorded date on which the participant was known to be alive. The FAS included all randomized participants. 9999 indicates that median, upper and lower limit of confidence interval were not estimable due to insufficient number of participants with events at study closure and due to limited duration of follow-up.

End point type	Secondary

End point timeframe:

From the date of randomization until death due to any cause, up to 35 months

End point values	Durvalumab + SoC	Placebo + SoC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	44		
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: OS in MRD+ Analysis Set

End point title	OS in MRD+ Analysis Set

End point description:

OS was defined as the time from the date of randomization until death due to any cause. Any participant not known to have died at the time of analysis was censored based on the last recorded date on which the participant was known to be alive. The MRD+ analysis set included all participants in the FAS who were MRD+, as determined by results from the post-surgical plasma sample based on the assay that was used at the time of randomization assay. 9999 indicates that median and upper limit of confidence interval were not estimable due to insufficient number of participants with events at study closure and due to limited duration of follow-up.

End point type	Secondary

End point timeframe:

From the date of randomization until death due to any cause, up to 35 months

End point values	Durvalumab + SoC: MRD+ Analysis Set	Placebo + SoC: MRD+ Analysis Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	11		
Units: months				
median (confidence interval 95%)	9999 (9.331 to 9999)	9999 (13.372 to 9999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment emergent adverse events(TEAEs) were collected from first dose of study treatment up to 90 days after last dose of study treatment, 19.1 months. All-cause mortality was assessed from start of randomization up to completion of study, 35 months.

Adverse event reporting additional description:

The safety analysis set consisted of all randomized participants who received at least 1 dose of study treatment (durvalumab/placebo and/or SoC chemotherapy).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Placebo + SoC

Reporting group description:

Participants received matching placebo via IV infusion in combination with SoC chemotherapy on Day 1 of each 3-week cycle for up to 4 cycles, followed by matching placebo continued on Day 1 of each 4-week cycle for up to 10 additional cycles until unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.
For participants with tumors of squamous histology, permitted SoC chemotherapy was a combination of carboplatin (AUC 6) and paclitaxel 200 mg/m^2 via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.
For participants with tumors of non-squamous tumor histology, permitted SoC chemotherapy regimens were pemetrexed 500 mg/m^2 in combination with either cisplatin 75 mg/m^2 or carboplatin AUC 5, all via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.

Reporting group title	Durvalumab + SoC

Reporting group description:

Participants received durvalumab 1500 mg via IV infusion in combination with SoC chemotherapy on Day 1 of each 3-week cycle for up to 4 cycles, followed by durvalumab monotherapy continued on Day 1 of each 4-week cycle for up to 10 additional cycles until unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.
For participants with tumors of squamous histology, permitted SoC chemotherapy was a combination of carboplatin (AUC 6) and paclitaxel 200 mg/m^2 via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.
For participants with tumors of non-squamous tumor histology, permitted SoC chemotherapy regimens were pemetrexed 500 mg/m^2 in combination with either cisplatin 75 mg/m^2 or carboplatin AUC 5, all via IV infusion on Day 1 of each 3-week cycle, for 4 cycles.

Serious adverse events	Placebo + SoC	Durvalumab + SoC	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 44 (22.73%)	14 / 45 (31.11%)	
number of deaths (all causes)	5	6	
number of deaths resulting from adverse events	1	1	
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Peripheral artery occlusion			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (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			
Pleural effusion			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary artery thrombosis			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Subdural haematoma			

subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Parkinson's disease			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
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			
Anaemia			
subjects affected / exposed	0 / 44 (0.00%)	2 / 45 (4.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Neutropenia			
subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 44 (0.00%)	3 / 45 (6.67%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Nausea			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Azotaemia			

subjects affected / exposed	1 / 44 (2.27%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	2 / 44 (4.55%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypopituitarism			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 44 (2.27%)	3 / 45 (6.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 44 (4.55%)	0 / 45 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Hyponatraemia			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	0 / 44 (0.00%)	1 / 45 (2.22%)	
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: 5 %

Non-serious adverse events	Placebo + SoC	Durvalumab + SoC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 44 (100.00%)	43 / 45 (95.56%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 44 (9.09%)	3 / 45 (6.67%)	
occurrences (all)	4	3	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	12 / 44 (27.27%)	15 / 45 (33.33%)	
occurrences (all)	13	18	
Asthenia			
subjects affected / exposed	4 / 44 (9.09%)	7 / 45 (15.56%)	
occurrences (all)	4	10	
Pyrexia			
subjects affected / exposed	2 / 44 (4.55%)	6 / 45 (13.33%)	
occurrences (all)	3	7	
Oedema peripheral			
subjects affected / exposed	3 / 44 (6.82%)	3 / 45 (6.67%)	
occurrences (all)	3	3	
Malaise			
subjects affected / exposed	3 / 44 (6.82%)	1 / 45 (2.22%)	
occurrences (all)	3	4	
Respiratory, thoracic and mediastinal disorders			

Hiccups			
subjects affected / exposed	4 / 44 (9.09%)	2 / 45 (4.44%)	
occurrences (all)	5	2	
Dyspnoea			
subjects affected / exposed	4 / 44 (9.09%)	4 / 45 (8.89%)	
occurrences (all)	4	5	
Cough			
subjects affected / exposed	5 / 44 (11.36%)	7 / 45 (15.56%)	
occurrences (all)	5	9	
Productive cough			
subjects affected / exposed	3 / 44 (6.82%)	3 / 45 (6.67%)	
occurrences (all)	3	3	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 44 (9.09%)	6 / 45 (13.33%)	
occurrences (all)	4	7	
Investigations			
Weight decreased			
subjects affected / exposed	3 / 44 (6.82%)	2 / 45 (4.44%)	
occurrences (all)	3	2	
Platelet count decreased			
subjects affected / exposed	2 / 44 (4.55%)	3 / 45 (6.67%)	
occurrences (all)	3	5	
Neutrophil count decreased			
subjects affected / exposed	5 / 44 (11.36%)	8 / 45 (17.78%)	
occurrences (all)	9	15	
White blood cell count decreased			
subjects affected / exposed	2 / 44 (4.55%)	7 / 45 (15.56%)	
occurrences (all)	5	10	
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	6 / 44 (13.64%)	1 / 45 (2.22%)	
occurrences (all)	6	1	
Paraesthesia			
subjects affected / exposed	3 / 44 (6.82%)	3 / 45 (6.67%)	
occurrences (all)	4	4	
Neuropathy peripheral			

subjects affected / exposed	5 / 44 (11.36%)	7 / 45 (15.56%)	
occurrences (all)	5	7	
Headache			
subjects affected / exposed	4 / 44 (9.09%)	8 / 45 (17.78%)	
occurrences (all)	6	9	
Dysgeusia			
subjects affected / exposed	2 / 44 (4.55%)	4 / 45 (8.89%)	
occurrences (all)	4	4	
Dizziness			
subjects affected / exposed	2 / 44 (4.55%)	4 / 45 (8.89%)	
occurrences (all)	4	4	
Anosmia			
subjects affected / exposed	0 / 44 (0.00%)	3 / 45 (6.67%)	
occurrences (all)	0	3	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	12 / 44 (27.27%)	15 / 45 (33.33%)	
occurrences (all)	13	21	
Neutropenia			
subjects affected / exposed	3 / 44 (6.82%)	8 / 45 (17.78%)	
occurrences (all)	5	10	
Thrombocytopenia			
subjects affected / exposed	1 / 44 (2.27%)	5 / 45 (11.11%)	
occurrences (all)	1	6	
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 44 (0.00%)	3 / 45 (6.67%)	
occurrences (all)	0	4	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	3 / 44 (6.82%)	5 / 45 (11.11%)	
occurrences (all)	7	8	
Stomatitis			
subjects affected / exposed	3 / 44 (6.82%)	3 / 45 (6.67%)	
occurrences (all)	3	3	
Nausea			

subjects affected / exposed	18 / 44 (40.91%)	19 / 45 (42.22%)	
occurrences (all)	35	32	
Gastrooesophageal reflux disease			
subjects affected / exposed	7 / 44 (15.91%)	1 / 45 (2.22%)	
occurrences (all)	7	1	
Dry mouth			
subjects affected / exposed	1 / 44 (2.27%)	3 / 45 (6.67%)	
occurrences (all)	1	3	
Abdominal pain			
subjects affected / exposed	2 / 44 (4.55%)	5 / 45 (11.11%)	
occurrences (all)	2	8	
Abdominal pain upper			
subjects affected / exposed	5 / 44 (11.36%)	0 / 45 (0.00%)	
occurrences (all)	6	0	
Constipation			
subjects affected / exposed	17 / 44 (38.64%)	12 / 45 (26.67%)	
occurrences (all)	24	15	
Diarrhoea			
subjects affected / exposed	7 / 44 (15.91%)	11 / 45 (24.44%)	
occurrences (all)	7	15	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	9 / 44 (20.45%)	13 / 45 (28.89%)	
occurrences (all)	10	13	
Dry skin			
subjects affected / exposed	3 / 44 (6.82%)	4 / 45 (8.89%)	
occurrences (all)	3	4	
Pruritus			
subjects affected / exposed	6 / 44 (13.64%)	6 / 45 (13.33%)	
occurrences (all)	8	8	
Rash			
subjects affected / exposed	5 / 44 (11.36%)	8 / 45 (17.78%)	
occurrences (all)	5	9	
Rash maculo-papular			
subjects affected / exposed	3 / 44 (6.82%)	3 / 45 (6.67%)	
occurrences (all)	3	3	

Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 44 (0.00%)	6 / 45 (13.33%)	
occurrences (all)	0	6	
Hypothyroidism			
subjects affected / exposed	1 / 44 (2.27%)	6 / 45 (13.33%)	
occurrences (all)	1	6	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	1 / 44 (2.27%)	3 / 45 (6.67%)	
occurrences (all)	1	4	
Back pain			
subjects affected / exposed	3 / 44 (6.82%)	5 / 45 (11.11%)	
occurrences (all)	3	6	
Arthralgia			
subjects affected / exposed	8 / 44 (18.18%)	7 / 45 (15.56%)	
occurrences (all)	13	7	
Pain in extremity			
subjects affected / exposed	4 / 44 (9.09%)	2 / 45 (4.44%)	
occurrences (all)	5	3	
Myalgia			
subjects affected / exposed	5 / 44 (11.36%)	4 / 45 (8.89%)	
occurrences (all)	12	4	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	3 / 44 (6.82%)	2 / 45 (4.44%)	
occurrences (all)	3	2	
Urinary tract infection			
subjects affected / exposed	1 / 44 (2.27%)	3 / 45 (6.67%)	
occurrences (all)	1	3	
COVID-19			
subjects affected / exposed	3 / 44 (6.82%)	3 / 45 (6.67%)	
occurrences (all)	3	3	
Metabolism and nutrition disorders			
Hypomagnesaemia			

subjects affected / exposed	3 / 44 (6.82%)	3 / 45 (6.67%)	
occurrences (all)	4	3	
Decreased appetite			
subjects affected / exposed	7 / 44 (15.91%)	9 / 45 (20.00%)	
occurrences (all)	11	14	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 April 2021	Removed secondary objectives and endpoints that were no longer considered necessary to analyze. Removed never smokers from the eligible population to reduce the probability of screen failure due to failure to meet the 50 variants required for MRD assessment. Changes were made to aspects of the screening procedures for simplification and clarification to provide flexibility during screening; and to reflect real world practice.
06 May 2021	Updated numbering in sections: Exclusion Criteria and Lifestyle Restrictions. Updated SAS definition. Clarified regarding prohibited prior radiotherapy.
02 August 2022	Revised planned analyses of objectives and endpoints based on the reduced sample size, following study enrollment closure on 25 May 2022. Removed text for long-term survival follow up. Updated end of study definition to account for early closure of study enrollment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Sponsor closed enrollment early due to changes in treatment landscape. Interpretation of efficacy results is inconclusive due to small sample size, resulting in wide confidence intervals, and limited follow-up. No new safety concerns were identified.

Notes: