Clinical trial results:
A Phase III, Randomized, Multicenter, Double-blind, Placebo-controlled Study of Durvalumab for the Treatment of Stage II-III NSCLC Patients with Minimal Residual Disease Following Surgery and Curative Intent Therapy (MERMAID-2)

Summary

EudraCT number	2020-000612-30
Trial protocol	DE PL NL GB BG BE FR GR HU CZ DK IT
Global end of trial date	15 January 2024

Results information

Result version number	v1 (current)
This version publication date	17 October 2024
First version publication date	17 October 2024

Trial information

Trial identification

Sponsor protocol code	D910MC00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04642469
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	15 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 January 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of durvalumab compared to placebo as measured by disease-free survival (DFS) in all randomized participants.

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 Council for Harmonisation/Good Clinical Practice, applicable regulatory requirements, and the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 November 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	France: 7
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Türkiye: 3
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Czechia: 1
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Japan: 5
Country: Number of subjects enrolled	Taiwan: 3
Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	Brazil: 1
Worldwide total number of subjects	30
EEA total number of subjects	15

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)	16
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This Phase III multicenter, double-blind, placebo-controlled study was conducted in participants with Stage II to III non-small cell lung cancer (NSCLC) at 21 sites in 13 countries.

Pre-assignment

Screening details:

30 participants were randomized in a 1:1 ratio to receive durvalumab monotherapy or placebo in the study.

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

Arm description:

Participants received durvalumab 1500 milligram (mg) via intravenous (IV) infusion over 60 minutes, once every 4 weeks (q4w) for a maximum of 26 cycles, 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	MEDI4736
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Durvalumab was provided in 500 mg vials. Participants received durvalumab 1500 mg via IV infusion over 60 minutes, q4w for a maximum of 26 cycles, unless protocol-specified discontinuation criterion was met.

Arm title	Placebo

Arm description:

Participants received matching placebo via IV infusion over 60 minutes, once q4w for a maximum of 26 cycles, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

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 in vials. Participants received matching placebo via IV infusion over 60 minutes, once q4w for a maximum of 26 cycles, unless protocol-specified discontinuation criterion was met.

Number of subjects in period 1	Durvalumab	Placebo
Started	15	15
Completed	0	1
Not completed	15	14
Adverse event, serious fatal	1	2
Consent withdrawn by subject	1	-
Failure to meet inclusion/exclusion criteria	1	-
Unspecified	1	1
Study/site closed following amendment 1	11	11

Baseline characteristics

Reporting groups	
Reporting group title	Durvalumab
Reporting group description:	
Participants received durvalumab 1500 milligram (mg) via intravenous (IV) infusion over 60 minutes, once every 4 weeks (q4w) for a maximum of 26 cycles, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo via IV infusion over 60 minutes, once q4w for a maximum of 26 cycles, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.	

Reporting group values	Durvalumab	Placebo	Total
Number of subjects	15	15	30
Age categorical Units: Subjects			
Adults (18-64 years)	11	5	16
From 65-84 years	4	10	14
Age Continuous Units: Years			
arithmetic mean	59.3	66.7	
standard deviation	± 8.6	± 10.3	-
Sex: Female, Male Units: Participants			
Female	7	4	11
Male	8	11	19
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	15	15	30
Race/Ethnicity, Customized Units: Subjects			
Asian	3	5	8
White	7	7	14
Other	1	0	1
Missing	4	3	7

End points

End points reporting groups

Reporting group title	Durvalumab

Reporting group description:

Participants received durvalumab 1500 milligram (mg) via intravenous (IV) infusion over 60 minutes, once every 4 weeks (q4w) for a maximum of 26 cycles, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

Reporting group title	Placebo

Reporting group description:

Participants received matching placebo via IV infusion over 60 minutes, once q4w for a maximum of 26 cycles, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

Primary: Disease-free survival (DFS)

End point title	Disease-free survival (DFS)[1]

End point description:

DFS was defined as the time from the date of randomization until any one of the following events, whichever occurred first: Date of disease recurrence using Investigator assessments according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 OR Date of death from any cause. The full analysis set (FAS) included all randomized participants. Here, '99999' indicates that upper limit of confidence interval was 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 8 weeks (q8w) ± 1 week until Week 48, then every 12 weeks (q12w) ± 1 week until appearance of RECIST 1.1-defined disease recurrence or follow-up, up to 16.6 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 analysis was descriptive in nature, no statistical analysis was reported.

End point values	Durvalumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: Months				
median (confidence interval 95%)	3.9 (3.515 to 99999)	2.0 (1.643 to 3.910)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An AE was any untoward medical occurrence (other than progression of the malignancy under evaluation) in a participant or clinical study participant administered a medicinal product and which did

not necessarily have causal relationship with this treatment. An SAE was an AE that occurred during any study phase and fulfilled one or more of following criteria: Resulted in death, was immediately life-threatening, required in-participant hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability or incapacity, was a congenital abnormality or birth defect, was an important medical event that might jeopardize the participant or might require medical treatment to prevent one of the outcomes listed above, AEs for malignant tumors reported during a study, malignant tumors that – as part of normal, if rare, progression–underwent transformation. Safety Analysis Set included all randomized participants who received any amount of study treatment.

End point type	Secondary

End point timeframe:

From start of study treatment (Day 1) up to 90 days after last dose of study treatment, approximately 21.4 months

End point values	Durvalumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	15		
Units: Participants				
Any AEs	13	10		
Any SAEs	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were collected from start of study treatment (Day 1) up to 90 days after last dose of study treatment, approximately 21.4 months. All-cause mortality=start of randomization (Day 0) up to completion of study, approximately 30 months.

Adverse event reporting additional description:

The Safety Analysis Set included all randomized participants who received any amount of study treatment. All-cause mortality was reported in FAS.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Durvalumab

Reporting group description:

Participants received durvalumab 1500 milligram (mg) via intravenous (IV) infusion over 60 minutes, once every 4 weeks (q4w) for a maximum of 26 cycles, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

Reporting group title	Placebo

Reporting group description:

Participants received matching placebo via IV infusion over 60 minutes, once q4w for a maximum of 26 cycles, unless there was unacceptable toxicity, withdrawal of consent, or another discontinuation criterion was met.

Serious adverse events	Durvalumab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Durvalumab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 14 (92.86%)	10 / 15 (66.67%)	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 14 (7.14%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Chest discomfort			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Asthenia			
subjects affected / exposed	3 / 14 (21.43%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Xerosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Tachyphrenia			

subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Investigations			
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Amylase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Platelet count decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Radiation pneumonitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 15 (13.33%)	
occurrences (all)	0	2	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hypoaesthesia			

subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Intercostal neuralgia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Memory impairment			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Presyncope			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Iron deficiency anaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	2 / 14 (14.29%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Periodontal disease			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Vomiting			

subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Skin exfoliation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	2 / 14 (14.29%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Pruritus			
subjects affected / exposed	3 / 14 (21.43%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Hypothyroidism			
subjects affected / exposed	4 / 14 (28.57%)	0 / 15 (0.00%)	
occurrences (all)	4	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Back pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

Musculoskeletal pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hepatitis C			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Diabetes mellitus			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hyperkalaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Hyperlipidaemia			

subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Hypermagnesaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 August 2022	The primary reason for this amendment was to close enrollment early, following the approval of neoadjuvant and adjuvant immunotherapy options for participants with resectable Stage II-III NSCLC. The amendment also provided procedures required for all participants who had signed informed consent for the study and ensured that eligible participants had access to open-label durvalumab where appropriate.

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.

The Sponsor closed enrollment to the study early due to treatment landscape changes. Interpretation of study outcomes were limited by the resulting small sample size and limited duration of follow-up.

Notes: