Clinical trial results:
A Phase 2 Open-label, Multicenter, Randomized, Multidrug Platform Study of Neoadjuvant Durvalumab Alone or in Combination with Novel Agents in Subjects with Resectable, Early-stage (I [> 2 cm] to IIIA) Non-small Cell Lung Cancer (NeoCOAST)

Summary

EudraCT number	2018-002932-26
Trial protocol	FR PT ES IT
Global end of trial date	13 January 2021

Results information

Result version number	v1 (current)
This version publication date	28 January 2022
First version publication date	28 January 2022

Trial information

Trial identification

Sponsor protocol code	D9108C00002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03794544
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Clinical Study Information Center
Sponsor organisation address	OneMedImmune Way, Gaithersburg, United States, MD 20878
Public contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 18772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 18772409479, 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 September 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the antitumor activity of durvalumab alone and/or in combination with novel agents.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating participant signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	Spain: 7
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	United States: 65
Worldwide total number of subjects	84
EEA total number of subjects	16

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)	32
From 65 to 84 years	50
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 84 participants were enrolled across 7 countries worldwide.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Durvalumab 1500 mg

Arm description:

Participants received durvalumab 1500 mg intravenously (IV) every 4 weeks (Q4W; on Week 1 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).

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 1500 mg was administered IV Q4W (on Week 1 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period.

Arm title	Durvalumab 1500 mg + Oleclumab 3000 mg

Arm description:

Participants received durvalumab 1500 mg IV Q4W (on Week 1 Day 1) and oleclumab 3000 mg IV every 2 weeks (Q2W; on Week 1 Day 1 and Week 3 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).

Arm type	Experimental
Investigational medicinal product name	Oleclumab
Investigational medicinal product code	MEDI9447
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Oleclumab 3000 mg was administered IV Q2W (on Week 1 Day 1 and Week 3 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period.

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	MEDI4736
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Durvalumab 1500 mg was administered IV Q4W (on Week 1 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period.

Arm title	Durvalumab 1500 mg + Monalizumab 750 mg

Arm description:

Participants received durvalumab 1500 mg IV Q4W (on Week 1 Day 1) and monalizumab 750 mg IV Q2W (on Week 1 Day 1 and Week 3 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).

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

Dosage and administration details:

Durvalumab 1500 mg was administered IV Q4W (on Week 1 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period.

Investigational medicinal product name	Monalizumab
Investigational medicinal product code	IPH2201
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Monalizumab 750 mg was administered IV Q2W (on Week 1 Day 1 and Week 3 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period.

Arm title	Durvalumab 1500 mg + Danvatirsen 200 mg

Arm description:

Participants received danvatirsen 200 mg IV on Days 1, 3, and 5 of Week 0 (7-day danvatirsen lead-in period), followed by durvalumab 1500 mg IV Q4W (on Week 1 Day 1) and danvatirsen 200 mg IV every week (on Week 1 Day 1, Week 2 Day 1, Week 3 Day 1, and Week 4 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).

Arm type	Experimental
Investigational medicinal product name	Danvatirsen
Investigational medicinal product code	AZD9150
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Danvatirsen 200 mg was administered IV on Days 1, 3, and 5 of Week 0 (7-day danvatirsen lead-in period), followed by every week (on Week 1 Day 1, Week 2 Day 1, Week 3 Day 1, and Week 4 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period.

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 1500 mg was administered IV Q4W (on Week 1 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period.

Number of subjects in period 1	Durvalumab 1500 mg	Durvalumab 1500 mg + Oleclumab 3000 mg	Durvalumab 1500 mg + Monalizumab 750 mg
Started	27	21	20
Treated	26	21	20
Completed	26	18	19
Not completed	1	3	1
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	1	1	-
Unspecified	-	1	-
Lost to follow-up	-	1	1

Number of subjects in period 1	Durvalumab 1500 mg + Danvatirsen 200 mg
Started	16
Treated	16
Completed	15
Not completed	1
Adverse event, serious fatal	1
Consent withdrawn by subject	-
Unspecified	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Durvalumab 1500 mg
Reporting group description:	
Participants received durvalumab 1500 mg intravenously (IV) every 4 weeks (Q4W; on Week 1 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).	
Reporting group title	Durvalumab 1500 mg + Oleclumab 3000 mg
Reporting group description:	
Participants received durvalumab 1500 mg IV Q4W (on Week 1 Day 1) and oleclumab 3000 mg IV every 2 weeks (Q2W; on Week 1 Day 1 and Week 3 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).	
Reporting group title	Durvalumab 1500 mg + Monalizumab 750 mg
Reporting group description:	
Participants received durvalumab 1500 mg IV Q4W (on Week 1 Day 1) and monalizumab 750 mg IV Q2W (on Week 1 Day 1 and Week 3 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).	
Reporting group title	Durvalumab 1500 mg + Danvatirsen 200 mg
Reporting group description:	
Participants received danvatirsen 200 mg IV on Days 1, 3, and 5 of Week 0 (7-day danvatirsen lead-in period), followed by durvalumab 1500 mg IV Q4W (on Week 1 Day 1) and danvatirsen 200 mg IV every week (on Week 1 Day 1, Week 2 Day 1, Week 3 Day 1, and Week 4 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).	

Reporting group values	Durvalumab 1500 mg	Durvalumab 1500 mg + Oleclumab 3000 mg	Durvalumab 1500 mg + Monalizumab 750 mg
Number of subjects	27	21	20
Age categorical Units: Subjects			
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)	11	10	10
From 65-84 years	16	11	10
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	67.1	65.5	65.1
standard deviation	± 9.0	± 7.5	± 6.3

Sex: Female, Male Units: Participants			
Female	13	9	6
Male	14	12	14
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	1	1
White	23	20	19
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	26	21	20
Unknown or Not Reported	0	0	0

Reporting group values	Durvalumab 1500 mg + Danvatirsen 200 mg	Total	
Number of subjects	16	84	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	1	32	
From 65-84 years	13	50	
85 years and over	2	2	
Age Continuous Units: Years			
arithmetic mean	72.9		
standard deviation	± 7.9	-	
Sex: Female, Male Units: Participants			
Female	6	34	
Male	10	50	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	2	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	5	
White	13	75	
More than one race	0	0	

Unknown or Not Reported	2	2	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	3	
Not Hispanic or Latino	14	81	
Unknown or Not Reported	0	0	

End points

End points reporting groups

Reporting group title	Durvalumab 1500 mg
Reporting group description:	
Participants received durvalumab 1500 mg intravenously (IV) every 4 weeks (Q4W; on Week 1 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).	
Reporting group title	Durvalumab 1500 mg + Oleclumab 3000 mg
Reporting group description:	
Participants received durvalumab 1500 mg IV Q4W (on Week 1 Day 1) and oleclumab 3000 mg IV every 2 weeks (Q2W; on Week 1 Day 1 and Week 3 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).	
Reporting group title	Durvalumab 1500 mg + Monalizumab 750 mg
Reporting group description:	
Participants received durvalumab 1500 mg IV Q4W (on Week 1 Day 1) and monalizumab 750 mg IV Q2W (on Week 1 Day 1 and Week 3 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).	
Reporting group title	Durvalumab 1500 mg + Danvatirsen 200 mg
Reporting group description:	
Participants received danvatirsen 200 mg IV on Days 1, 3, and 5 of Week 0 (7-day danvatirsen lead-in period), followed by durvalumab 1500 mg IV Q4W (on Week 1 Day 1) and danvatirsen 200 mg IV every week (on Week 1 Day 1, Week 2 Day 1, Week 3 Day 1, and Week 4 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).	

Primary: Major Pathological Response Rate

End point title	Major Pathological Response Rate[1]
End point description:	
Major pathological response rate is defined as percentage of participants with <=10% residual viable tumor cells in the resected specimen. Intent-to-treat (ITT) population was analysed which included participants who were randomized and were analyzed according to their randomized treatment group.	
End point type	Primary
End point timeframe:	
Day 1 through Day 42	

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: Statistical analysis was not applicable since there were no inferential statistics, only descriptive statistics were performed for this end point.

End point values	Durvalumab 1500 mg	Durvalumab 1500 mg + Oleclumab 3000 mg	Durvalumab 1500 mg + Monalizumab 750 mg	Durvalumab 1500 mg + Danvatirsen 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	21	20	16
Units: Percentage of participants				
number (confidence interval 95%)	11.1 (2.4 to	19.0 (5.4 to	30.0 (11.9 to	31.3 (11.0 to

29.2)	41.9)	54.3)	58.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Pathological Complete Response (pCR) Rate

End point title	Pathological Complete Response (pCR) Rate

End point description:

The pCR rate is defined as percentage of participants with no residual viable tumor cells in the resected specimen. The ITT population was analysed which included participants who were randomized and were analyzed according to their randomized treatment group.

End point type	Secondary

End point timeframe:

Day 1 through Day 42

End point values	Durvalumab 1500 mg	Durvalumab 1500 mg + Oleclumab 3000 mg	Durvalumab 1500 mg + Monalizumab 750 mg	Durvalumab 1500 mg + Danvatirsen 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	27	21	20	16
Units: Percentage of participants				
number (confidence interval 95%)	3.7 (0.1 to 19.0)	9.5 (1.2 to 30.4)	10.0 (1.2 to 31.7)	12.5 (1.6 to 38.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Feasibility to Surgery

End point title	Feasibility to Surgery

End point description:

Feasibility to surgery is defined as the percentage of participants who underwent the planned surgery within Days 29 to 42 after Week 1 Day 1. As-treated population was analysed which included all participants who received any study drug and analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 29 to Day 42 after Week 1 Day 1

End point values	Durvalumab 1500 mg	Durvalumab 1500 mg + Oleclumab 3000 mg	Durvalumab 1500 mg + Monalizumab 750 mg	Durvalumab 1500 mg + Danvatirsen 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	21	20	16
Units: Percentage of participants				
number (not applicable)	84.6	81.0	90.0	93.8

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. The TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. As-treated population was analysed which included all participants who received any study drug and analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

From Day 1 through Day 105

End point values	Durvalumab 1500 mg	Durvalumab 1500 mg + Oleclumab 3000 mg	Durvalumab 1500 mg + Monalizumab 750 mg	Durvalumab 1500 mg + Danvatirsen 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	21	20	16
Units: Participants				
Any TEAEs	18	19	15	13
Any TESAEs	3	2	1	5

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Grade 3 or Grade 4 Clinical Laboratory Toxicities

End point title	Number of Participants With Grade 3 or Grade 4 Clinical Laboratory Toxicities

End point description:

Participants with Grade 3 or Grade 4 clinical laboratory toxicities are reported. Laboratory tests included hematology, coagulation, chemistry, and urinalysis. As-treated population was analysed which included all participants who received any study drug and analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

From Day 1 through Day 105

End point values	Durvalumab 1500 mg	Durvalumab 1500 mg + Oleclumab 3000 mg	Durvalumab 1500 mg + Monalizumab 750 mg	Durvalumab 1500 mg + Danvatirsen 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	21	20	16
Units: Participants				
Alanine aminotransferase increased	0	0	0	2
Gamma glutamyl transferase increased	0	0	0	1
Lipase increased	1	1	1	0
Hyponatremia	2	0	0	0
Lymphocyte count decreased	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Vital Signs Reported as TEAEs

End point title	Number of Participants With Abnormal Vital Signs Reported as TEAEs

End point description:

Participants with abnormal vital sign reported as TEAEs are reported. As-treated population was analysed which included all participants who received any study drug and analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

From Day 1 through Day 105

End point values	Durvalumab 1500 mg	Durvalumab 1500 mg + Oleclumab 3000 mg	Durvalumab 1500 mg + Monalizumab 750 mg	Durvalumab 1500 mg + Danvatirsen 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	21	20	16
Units: Participants				
Palpitations	1	0	0	0
Pyrexia	1	2	1	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 through Day 105

Adverse event reporting additional description:

As-treated population was considered for collecting AEs data. As-treated population included all participants who received any study drug and analyzed according to the treatment they actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Durvalumab 1500 mg

Reporting group description:

Participants received durvalumab 1500 mg intravenously (IV) every 4 weeks (Q4W; on Week 1 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).

Reporting group title	Durvalumab 1500 mg + Oleclumab 3000 mg

Reporting group description:

Participants received durvalumab 1500 mg IV Q4W (on Week 1 Day 1) and oleclumab 3000 mg IV every 2 weeks (Q2W; on Week 1 Day 1 and Week 3 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).

Reporting group title	Durvalumab 1500 mg + Monalizumab 750 mg

Reporting group description:

Participants received durvalumab 1500 mg IV Q4W (on Week 1 Day 1) and monalizumab 750 mg IV Q2W (on Week 1 Day 1 and Week 3 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).

Reporting group title	Durvalumab 1500 mg + Danvatirsen 200 mg

Reporting group description:

Participants received danvatirsen 200 mg IV on Days 1, 3, and 5 of Week 0 (7-day danvatirsen lead-in period), followed by durvalumab 1500 mg IV Q4W (on Week 1 Day 1) and danvatirsen 200 mg IV every week (on Week 1 Day 1, Week 2 Day 1, Week 3 Day 1, and Week 4 Day 1) until disease progression, unacceptable toxicity, or other reason of treatment discontinuation over a 28-day treatment period. Surgical resection was planned between Day 29 and Day 42. After surgical resection, participants were followed up to Day 105 (starting from Week 1 Day 1).

Serious adverse events	Durvalumab 1500 mg	Durvalumab 1500 mg + Oleclumab 3000 mg	Durvalumab 1500 mg + Monalizumab 750 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 26 (11.54%)	2 / 21 (9.52%)	1 / 20 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			

Bronchial anastomosis complication			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural haemorrhage			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Pericarditis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Haemothorax			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary air leakage			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal infarct			

subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Immune-mediated arthritis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 26 (3.85%)	1 / 21 (4.76%)	0 / 20 (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
Wound infection			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Durvalumab 1500 mg + Danvatirsen 200 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 16 (31.25%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Bronchial anastomosis complication			

subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Procedural haemorrhage				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Pericarditis				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Haemothorax				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary air leakage				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal infarct				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Musculoskeletal and connective tissue disorders			
Immune-mediated arthritis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Covid-19			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Durvalumab 1500 mg	Durvalumab 1500 mg + Oleclumab 3000 mg	Durvalumab 1500 mg + Monalizumab 750 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 26 (69.23%)	19 / 21 (90.48%)	14 / 20 (70.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			

Embolism			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	3 / 26 (11.54%)	3 / 21 (14.29%)	0 / 20 (0.00%)
occurrences (all)	3	3	0
Fatigue			
subjects affected / exposed	6 / 26 (23.08%)	4 / 21 (19.05%)	2 / 20 (10.00%)
occurrences (all)	6	4	2
Facial pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Generalised oedema			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 26 (3.85%)	2 / 21 (9.52%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	1 / 26 (3.85%)	3 / 21 (14.29%)	1 / 20 (5.00%)
occurrences (all)	1	3	1
Epistaxis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	3 / 26 (11.54%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	3	1	0
Haemoptysis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Pneumonitis			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Nasal obstruction			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Productive cough			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 26 (7.69%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	2	1	0
Depression			
subjects affected / exposed	2 / 26 (7.69%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Insomnia			

subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Emotional distress			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Investigations			
Amylase increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 26 (3.85%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 26 (3.85%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Blood bilirubin increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 26 (0.00%)	2 / 21 (9.52%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			

subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
International normalised ratio decreased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Tri-iodothyronine increased			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Prothrombin time shortened			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	0	1	1
Weight decreased			
subjects affected / exposed	0 / 26 (0.00%)	2 / 21 (9.52%)	0 / 20 (0.00%)
occurrences (all)	0	2	0
Injury, poisoning and procedural complications			
Post procedural discomfort			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Fall			

subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	5 / 26 (19.23%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	5	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Transient ischaemic attack			

subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Vocal cord paresis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Nephrogenic anaemia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Neutropenia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 26 (3.85%)	1 / 21 (4.76%)	2 / 20 (10.00%)
occurrences (all)	1	1	2
Diarrhoea			
subjects affected / exposed	1 / 26 (3.85%)	2 / 21 (9.52%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
Dyspepsia			

subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	2 / 26 (7.69%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Nausea			
subjects affected / exposed	2 / 26 (7.69%)	3 / 21 (14.29%)	0 / 20 (0.00%)
occurrences (all)	2	3	0
Oral pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Onychoclasis			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0

Pruritus			
subjects affected / exposed	0 / 26 (0.00%)	2 / 21 (9.52%)	2 / 20 (10.00%)
occurrences (all)	0	2	2
Rash maculo-papular			
subjects affected / exposed	1 / 26 (3.85%)	1 / 21 (4.76%)	1 / 20 (5.00%)
occurrences (all)	1	1	1
Rash			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Scar pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Rash pruritic			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Skin discolouration			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Arthralgia			
subjects affected / exposed	2 / 26 (7.69%)	2 / 21 (9.52%)	0 / 20 (0.00%)
occurrences (all)	2	2	0
Bone pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0

Joint swelling			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Chest wall mass			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Muscle tightness			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	2 / 26 (7.69%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Myalgia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Chest wall abscess			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Influenza			

subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	2 / 20 (10.00%)
occurrences (all)	0	1	2
Urinary tract infection			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Covid-19			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 26 (11.54%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 26 (0.00%)	1 / 21 (4.76%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	1 / 26 (3.85%)	2 / 21 (9.52%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Hypomagnesaemia			
subjects affected / exposed	1 / 26 (3.85%)	0 / 21 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Hyponatraemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 21 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1

Non-serious adverse events	Durvalumab 1500 mg + Danvatirsen 200 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 16 (81.25%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Embolism			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hot flush			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Facial pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Generalised oedema			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	2		
Non-cardiac chest pain			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	3 / 16 (18.75%)		
occurrences (all)	3		
Haemoptysis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pneumonitis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nasal obstruction			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Rhinitis allergic			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Productive cough			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Emotional distress			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Investigations			
Amylase increased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Alanine aminotransferase increased			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood bicarbonate decreased			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Blood bilirubin increased			

subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood thyroid stimulating hormone decreased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Blood lactate dehydrogenase increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
International normalised ratio decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Hepatic enzyme increased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Lymphocyte count decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Neutrophil count decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Platelet count decreased				
subjects affected / exposed	1 / 16 (6.25%)			
occurrences (all)	1			
Tri-iodothyronine increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Transaminases increased				
subjects affected / exposed	0 / 16 (0.00%)			
occurrences (all)	0			
Prothrombin time shortened				

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Post procedural discomfort			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Paraesthesia			

subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Sciatica			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Transient ischaemic attack			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Vocal cord paresis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Nephrogenic anaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Vitreous floaters			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Visual impairment			

subjects affected / exposed occurrences (all)	1 / 16 (6.25%) 1		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	 0 / 16 (0.00%) 0		
Diarrhoea subjects affected / exposed occurrences (all)	 0 / 16 (0.00%) 0		
Dyspepsia subjects affected / exposed occurrences (all)	 0 / 16 (0.00%) 0		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	 2 / 16 (12.50%) 2		
Haemorrhoids subjects affected / exposed occurrences (all)	 0 / 16 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1		
Oral pain subjects affected / exposed occurrences (all)	 0 / 16 (0.00%) 0		
Stomatitis subjects affected / exposed occurrences (all)	 0 / 16 (0.00%) 0		
Toothache subjects affected / exposed occurrences (all)	 1 / 16 (6.25%) 1		
Vomiting subjects affected / exposed occurrences (all)	 0 / 16 (0.00%) 0		
Skin and subcutaneous tissue disorders Dermatitis			

subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Onychoclasis			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	2 / 16 (12.50%)		
occurrences (all)	2		
Rash maculo-papular			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Scar pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Rash pruritic			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Skin discolouration			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hypothyroidism			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Bone pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Chest wall mass			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Muscle tightness			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Neck pain			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Osteoarthritis			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Infections and infestations			
Chest wall abscess			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Herpes zoster			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Covid-19			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Diabetes mellitus			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			

subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	1 / 16 (6.25%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	0 / 16 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2018	Doses should be omitted, and therapy may be discontinued at the discretion of the investigator, for toxicities that occurred in participants treated with durvalumab + oleclumab (>= Grade 2 pulmonary oedema or >= Grade 3 peripheral oedema). Electrocardiogram (ECG) assessments were added pre dose and immediately after the end of danvatirsen infusion on Week 0 Day 1 and Week 3 Day 1, respectively, and as clinically indicated. Pharmacokinetic assessments were added on Week 3, Day 1 to align with ECG assessments. The SRC would assess feasibility to surgery for all treatment arms and added safety measures in the event that one participant per treatment arm experienced a delay in receiving planned surgery.
18 January 2019	Participant population was revised to include participants with N2 disease (one single nodal station <= 3 cm only). Forced expiratory volume in one second and Diffusing capacity of the lungs for carbon monoxide requirements were revised from >= 60% to >= 50%. Participants who had a curative treated malignancy with no known active disease for > 2 years before enrolment on the study were eligible to enroll into this study. Monalizumab dose preparation, administration, and manufacturing process was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
13 April 2020	The trial was interrupted due to COVID-19 pandemic.	07 May 2020

Notes:

Limitations and caveats

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

The pharmacokinetic and immunogenicity samples are still being analyzed. Results for these outcome measures will be posted by 30Jun2022.

Notes: