Clinical trial results:
A Phase 2, Open-label, Multicenter, Randomized, Multidrug Platform Study of Durvalumab Alone or in Combination with Novel Agents in Subjects with Locally Advanced, Unresectable, Stage III Non-small Cell Lung Cancer (COAST)

Summary

EudraCT number	2018-002931-35
Trial protocol	FR PT ES PL IT
Global end of trial date	18 July 2023

Results information

Result version number	v1 (current)
This version publication date	25 July 2024
First version publication date	25 July 2024

Trial information

Trial identification

Sponsor protocol code	D9108C00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03822351
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca Clinical Study Information Center
Sponsor organisation address	One MedImmune Way, Gaithersburg, United States, 20878
Public contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +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	13 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 July 2023
Global end of trial reached?	Yes
Global end of trial date	18 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the antitumor activity of durvalumab alone vs durvalumab in combination with novel agents by calculating the Objective Response rate (ORR) per Response Evaluation Criteria for Solid Tumors version 1.1

Protection of trial subjects:

Each subject was assigned a SID to ensure that personally identifiable information is kept separate from the study data. Subject data that are relevant to the study, eg, demographic information, physical or mental health condition, diagnosis, comorbidities, laboratory test results, etc will only be collected with the subject's informed consent. The informed consent form will incorporate (or, in some cases, be accompanied by a separate document incorporating) wording that describes how subject data will be collected, used, and distributed in compliance with relevant data protection and privacy legislation. Data (clinical and biological sample) from this study may be used and may be combined with results from other studies for additional scientific-related research, based on agreement from the subject as defined in the informed consent form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 December 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	France: 39
Country: Number of subjects enrolled	Hong Kong: 6
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Portugal: 6
Country: Number of subjects enrolled	Spain: 53
Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	United States: 71
Worldwide total number of subjects	189
EEA total number of subjects	104

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)	87
From 65 to 84 years	101
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

A total of 258 participants were enrolled in 60 study centers across 8 countries worldwide. 69 participants were not randomized (screen failures) and 189 participants were randomized (1:1:1) to receive either durvalumab monotherapy (n=67); or durvalumab + oleclumab (n=60); or durvalumab + monalizumab (n=62).

Pre-assignment

Screening details:

The first participant was randomized into the study on 3 January 2019 and the last participant was randomized on 6 July 2020.
After randomization, 3 participants (1 from each arm) were deemed not eligible and did not receive treatment.

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	Control Arm (durvalumab monotherapy)

Arm description:

Durvalumab 1500 mg IV monotherapy Q4W

Arm type	Active comparator
Investigational medicinal product name	Durvalumab
Investigational medicinal product code	MEDI4736
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Durvalumab 1500 mg IV monotherapy Q4W

Arm title	Arm A (durvalumab + oleclumab)

Arm description:

Durvalumab 1500 mg IV Q4W + Oleclumab 3000 mg IV (Q2W for cycles 1 and 2, then Q4W starting cycle 3)

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

Dosage and administration details:

Oleclumab 3000 mg IV (Q2W for cycles 1 and 2, then Q4W starting cycle 3)

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	MEDI4736
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Durvalumab 1500 mg IV monotherapy Q4W

Arm title	Arm B (durvalumab + monalizumab)
Arm description: Durvalumab 1500 mg IV Q4W + Monalizumab 750 mg IV Q2W	
Arm type	Experimental
Investigational medicinal product name	Monalizumab
Investigational medicinal product code	IPH2201
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: Monalizumab 750 mg IV Q2W	
Investigational medicinal product name	Durvalumab
Investigational medicinal product code	MEDI4736
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details: Durvalumab 1500 mg IV monotherapy Q4W	

Number of subjects in period 1	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)
Started	67	60	62
Completed	21	29	30
Not completed	46	31	32
Consent withdrawn by subject	10	4	6
Death	27	23	24
Progressive Disease	2	1	-
Lost to follow-up	6	2	1
Not treated	1	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Control Arm (durvalumab monotherapy)
Reporting group description:	
Durvalumab 1500 mg IV monotherapy Q4W	
Reporting group title	Arm A (durvalumab + oleclumab)
Reporting group description:	
Durvalumab 1500 mg IV Q4W + Oleclumab 3000 mg IV (Q2W for cycles 1 and 2, then Q4W starting cycle 3)	
Reporting group title	Arm B (durvalumab + monalizumab)
Reporting group description:	
Durvalumab 1500 mg IV Q4W + Monalizumab 750 mg IV Q2W	

Reporting group values	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)
Number of subjects	67	60	62
Age categorical Units: Subjects			
Adults (18-64 years)	30	29	28
From 65-84 years	37	31	33
85 years and over	0	0	1
Age Continuous Units: years			
median	66	65	65
full range (min-max)	46 to 81	37 to 83	44 to 87
Sex: Female, Male Units: Participants			
Female	22	18	20
Male	45	42	42
Region of Enrollment Units: Subjects			
Canada	3	2	1
France	15	19	5
Hong-Kong	1	2	3
Italy	0	3	3
Portugal	3	0	3
Spain	19	12	22
Taiwan	1	0	1
United States	25	22	24
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	3	2
Not Hispanic or Latino	63	56	59
Unknown	1	1	1
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	5	4	5

Black or African American	1	5	2
Native Hawaiian or Other Pacific Islander	1	0	0
White	57	47	55
Other	1	2	0
Missing	2	1	0

Reporting group values	Total		
Number of subjects	189		
Age categorical Units: Subjects			
Adults (18-64 years)	87		
From 65-84 years	101		
85 years and over	1		
Age Continuous Units: years median full range (min-max)	--		
Sex: Female, Male Units: Participants			
Female	60		
Male	129		
Region of Enrollment Units: Subjects			
Canada	6		
France	39		
Hong-Kong	6		
Italy	6		
Portugal	6		
Spain	53		
Taiwan	2		
United States	71		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	8		
Not Hispanic or Latino	178		
Unknown	3		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1		
Asian	14		
Black or African American	8		
Native Hawaiian or Other Pacific Islander	1		
White	159		
Other	3		
Missing	3		

Subject analysis sets

Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The Intent-to-treat (ITT) population included participants who were randomized and were analyzed according to their randomized treatment group

Subject analysis set title	As-treated Population
Subject analysis set type	Safety analysis

Subject analysis set description:

The As-treated population included all participants who receive any IP. Participants were analyzed according to the treatment they received

Reporting group values	ITT Population	As-treated Population	
Number of subjects	189	186	
Age categorical Units: Subjects			
Adults (18-64 years)	87	85	
From 65-84 years	101	100	
85 years and over	1	1	
Age Continuous Units: years			
median	65	65	
full range (min-max)	37 to 87	37 to 87	
Sex: Female, Male Units: Participants			
Female	60	59	
Male	129	127	
Region of Enrollment Units: Subjects			
Canada	6	6	
France	39	39	
Hong-Kong	6	6	
Italy	6	6	
Portugal	6	6	
Spain	53	51	
Taiwan	2	2	
United States	71	70	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	8	8	
Not Hispanic or Latino	178	175	
Unknown	3	3	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	14	14	
Black or African American	8	8	
Native Hawaiian or Other Pacific Islander	1	1	
White	159	156	
Other	3	3	
Missing	3	3	

End points

End points reporting groups

Reporting group title	Control Arm (durvalumab monotherapy)
Reporting group description:	
Durvalumab 1500 mg IV monotherapy Q4W	
Reporting group title	Arm A (durvalumab + oleclumab)
Reporting group description:	
Durvalumab 1500 mg IV Q4W + Oleclumab 3000 mg IV (Q2W for cycles 1 and 2, then Q4W starting cycle 3)	
Reporting group title	Arm B (durvalumab + monalizumab)
Reporting group description:	
Durvalumab 1500 mg IV Q4W + Monalizumab 750 mg IV Q2W	
Subject analysis set title	ITT Population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The Intent-to-treat (ITT) population included participants who were randomized and were analyzed according to their randomized treatment group	
Subject analysis set title	As-treated Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The As-treated population included all participants who receive any IP. Participants were analyzed according to the treatment they received	

Primary: Objective Response (OR) rate as a measure of antitumor activity of durvalumab alone vs durvalumab in combination with novel agents

End point title	Objective Response (OR) rate as a measure of antitumor activity of durvalumab alone vs durvalumab in combination with novel agents[1]
End point description:	
ORR was defined as the percentage of participants with at least one visit response of Complete Response (CR) or Partial Response (PR) per RECIST 1.1 for target lesions: CR: Disappearance of all target lesions; PR: >=30% decrease in the sum of the longest diameter of target lesions; OR = CR + PR.	
End point type	Primary
End point timeframe:	
ORR at 16 weeks after randomization is the timing for radiologic assessment of the primary endpoint	
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: This should not be required for COAST.	

End point values	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	60	62	
Units: Percentage of Participants				
number (confidence interval 95%)	23.9 (14.3 to 35.9)	35.0 (23.1 to 48.4)	40.3 (28.1 to 53.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Adverse Events as a measure of safety and tolerability of durvalumab alone and in combination with novel agents

End point title	Incidence of Adverse Events as a measure of safety and tolerability of durvalumab alone and in combination with novel agents

End point description:

The secondary endpoint of safety as assessed by the presence of adverse events and serious adverse events

End point type	Secondary

End point timeframe:

From time of informed consent through treatment period (12 months) or up to 3 months post last dose of study treatment

End point values	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	66	59	61	
Units: Participants				
Participants with any TEAEs	65	57	61	
Participants with any serious TEAEs	23	20	17	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of clinically significant laboratory values as a measure of safety and tolerability of durvalumab alone and in combination with novel agents

End point title	Incidence of clinically significant laboratory values as a measure of safety and tolerability of durvalumab alone and in combination with novel agents

End point description:

The secondary endpoint of safety as assessed by the presence of Grade 3 or 4 clinical laboratory toxicities (based on NCI-CTCAE v5.0) in chemistry and hematology values observed from treatment initiation up to and including 3 months post end of treatment.

End point type	Secondary

End point timeframe:

From baseline through treatment up to 5 years after first treatment

End point values	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	66	59	61	
Units: Participants				
Alanine Aminostransferase (U/L) toxicities	1	0	0	
Albumin (g/dL) toxicities	2	0	0	
Amylase (U/L) toxicities	1	0	2	
Aspartate Aminotransferase (U/L) toxicities	1	0	1	
Creatinine (mg/dL) toxicities	1	0	0	
Creatinine Clearance Rate (mL/min) toxicities	2	1	0	
Gamma Glutamyl Transferase (U/L) toxicities	1	0	0	
Any Grade 3 or 4 Hyperkalemia (mEq/L) toxicities	0	0	2	
Hypokalemia (mEq/L) toxicities	1	0	1	
Hypocalcemia (corrected) (mg/dL) toxicities	1	0	0	
Hypernatremia (mEq/L) toxicities	1	2	1	
Lipase (U/L) toxicities	1	4	2	
Hemoglobin increased (g/dL) toxicities	3	0	0	
Lymphocyte count increased (10^3/uL) toxicities	19	11	11	
Platelet count decreased (10^3/uL) toxicities	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of abnormalities in Vital Signs as a measure of safety and tolerability of durvalumab alone and in combination with novel agents

End point title	Incidence of abnormalities in Vital Signs as a measure of safety and tolerability of durvalumab alone and in combination with novel agents

End point description:

The secondary endpoint of safety as assessed by the presence of abnormal vital signs reported as adverse events from treatment initiation up to and including 3 months post end of treatment.

End point type	Secondary

End point timeframe:

From baseline through treatment up to 5 years after first treatment

End point values	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	66	59	61	
Units: Participants				
Hypertension	3	3	0	
Hypotension	2	0	3	
Palpitations	0	0	1	
Pyrexia	6	8	10	
Tachycardia	1	2	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR) as a measure of efficacy of durvalumab alone vs durvalumab in combination with novel agents

End point title	Duration of Response (DoR) as a measure of efficacy of durvalumab alone vs durvalumab in combination with novel agents

End point description:

The duration from the first documentation of a subsequently confirmed OR to the first documentation of a disease progression according to RECIST v1.1 or death due to any cause, whichever occurs first. Only subjects who have achieved OR (confirmed CR or confirmed PR) will be evaluated for DoR

End point type	Secondary

End point timeframe:

From time of first documented response until disease progression or up to a maximum of 5 years after randomization

End point values	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	21	25	
Units: Months				
median (confidence interval 95%)	99999 (14.1 to 99999)	29.9 (17.1 to 99999)	23.0 (10.2 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control (DC) as a measure of efficacy of durvalumab alone vs durvalumab in combination with novel agents

End point title	Disease Control (DC) as a measure of efficacy of durvalumab alone vs durvalumab in combination with novel agents

End point description:

Disease control rate (DCR) was defined as the proportion of subjects with a BOR of confirmed CR, confirmed PR, or SD (maintained for ≥ 16 weeks) based on RECIST v1.1.

End point type	Secondary

End point timeframe:

From time of randomization until disease progression or up to a maximum of 5 years

End point values	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	60	62	
Units: Percentage of patients				
number (confidence interval 95%)	58.2 (45.5 to 70.2)	80.0 (67.7 to 89.2)	79.0 (66.8 to 88.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) as a measure of efficacy of durvalumab alone vs durvalumab in combination with novel agents

End point title	Progression-Free Survival (PFS) as a measure of efficacy of durvalumab alone vs durvalumab in combination with novel agents

End point description:

From randomization until the first documentation of disease progression according to RECIST v1.1 or death due to any cause, whichever occurs first

End point type	Secondary

End point timeframe:

From time of randomization until disease progression or up to a maximum of 5 years

End point values	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	60	62	
Units: Months				
median (confidence interval 95%)	7.3 (4.0 to 13.8)	21.1 (10.4 to 30.9)	19.8 (13.6 to 31.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) as a measure of efficacy of durvalumab alone vs durvalumab in combination with novel agents

End point title	Overall Survival (OS) as a measure of efficacy of durvalumab alone vs durvalumab in combination with novel agents

End point description:

OS was defined as the time from the date of randomization until death due to any cause. Assessed until 18-July-2023 data cut-off, providing a follow-up to a maximum of approximately 2 years.

End point type	Secondary

End point timeframe:

From time of randomization until death due to any cause or up to a maximum of 5 years

End point values	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	60	62	
Units: Months				
median (confidence interval 95%)	40.9 (22.6 to 99999)	99999 (31.9 to 99999)	99999 (31.3 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival 12 month landmark rate (PFS-12) as a measure of efficacy of durvalumab alone vs durvalumab in combination with novel agents

End point title	Progression-Free Survival 12 month landmark rate (PFS-12) as a measure of efficacy of durvalumab alone vs durvalumab in combination with novel agents

End point description:

PFS-12 was defined as the percentage of participants who were alive and progression free at 12 months after randomization.

End point type	Secondary

End point timeframe:

PFS at 12 months after randomization

End point values	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	67	60	62	
Units: Percentage of Participants				
number (confidence interval 95%)	37.6 (24.7 to 50.4)	63.5 (49.2 to 74.7)	73.2 (59.6 to 82.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of durvalumab alone and in combination with novel agents

End point title	Pharmacokinetics of durvalumab alone and in combination with novel agents

End point description:

The PK samples for durvalumab were collected at prespecified time points: Cycle 1 Day 1 (pre-dose), Cycle 1 Day 1 (EOI), Cycle 2 Day 1 (pre-dose), Cycle 7 Day 1 (pre-dose), Cycle 11 Day 1 (pre-dose), every 8 weeks follow-up (10 months post
Cycle 1 Day 1 only), and every 12 weeks follow-up (Month 15 only).

End point type	Secondary

End point timeframe:

From randomization up to 15 months after first treatment

End point values	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	41	51	
Units: Micrograms per milliliter				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1: End of Infusion	318.0 (± 199.6)	277.4 (± 316.1)	223.7 (± 1272)	
Cycle 2 Day 1: Pre-Dose	59.7 (± 58.6)	68.0 (± 49.9)	74.3 (± 40.7)	
Cycle 7 Day 1: Pre-Dose	151.6 (± 37.7)	127.9 (± 66.4)	176.5 (± 45.6)	
Cycle 11 Day 1: Pre-Dose	156.7 (± 50.0)	146.5 (± 91.3)	172.4 (± 40.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics of novel agents in combination with durvalumab

End point title	Pharmacokinetics of novel agents in combination with durvalumab[2]

End point description:

The PK samples for oleclumab and monalizumab were collected at prespecified time points: Cycle 1 Day 1 (pre-dose), Cycle 1 Day 1 (EOI), Cycle 2 Day 1 (pre-dose), Cycle 7 Day 1 (pre-dose), Cycle 11 Day 1 (pre-dose), every 8 weeks follow-up (10 months post
Cycle 1 Day 1 only), and every 12 weeks follow-up (Month 15 only).

End point type	Secondary

End point timeframe:

From randomization up to 15 months after first treatment

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Because this is only for combination arms

End point values	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: Micrograms per milliliter				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1: End of Infusion	581.6 (± 210.5)	160.0 (± 286.4)		
Cycle 2 Day 1: Pre-Dose	216.4 (± 58.6)	102.6 (± 39.2)		
Cycle 7 Day 1: Pre-Dose	124.5 (± 109.0)	194.5 (± 33.8)		
Cycle 11 Day 1: Pre-Dose	132.0 (± 166.8)	196.2 (± 48.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Development of detectable Anti-Drug Antibody (ADA) response to durvalumab alone and in combination with novel agents

End point title	Development of detectable Anti-Drug Antibody (ADA) response to durvalumab alone and in combination with novel agents

End point description:

ADA positive post-baseline only was also referred to as treatment-induced ADA positive. Treatment-boosted ADA was defined as baseline positive ADA titer that was boosted to a 4-fold or higher following drug administration. Persistently positive was defined as positive at ≥2 post-baseline assessments (with ≥16 weeks between first and last positive) or positive at last post-baseline assessment. Transiently positive was defined as having at least 1 post-baseline ADA positive assessment and not fulfilling the conditions of persistently positive.

End point type	Secondary

End point timeframe:

From randomization up to 15 months after first treatment

End point values	Control Arm (durvalumab monotherapy)	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	18	33	
Units: Participants				
ADA positive at any visit (ADA prevalence)	3	1	2	

Treatment-emergent ADA positive (ADA incidence)	1	0	0	
Treatment-boosted ADA	0	0	0	
Treatment-induced ADA	1	0	0	
ADA positive at baseline only	2	1	2	
ADA positive post-baseline and at baseline	0	0	0	
Persistently positive	1	0	0	
Transiently positive	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Development of detectable Anti-Drug Antibody (ADA) response to novel agents in combination with durvalumab

End point title	Development of detectable Anti-Drug Antibody (ADA) response to novel agents in combination with durvalumab[3]

End point description:

ADA positive post-baseline only was also referred to as treatment-induced ADA positive. Treatment-boosted ADA was defined as baseline positive ADA titer that was boosted to a 4-fold or higher following drug administration. Persistently positive was defined as positive at ≥2 post-baseline assessments (with ≥16 weeks between first and last positive) or positive at last post-baseline assessment. Transiently positive was defined as having at least 1 post-baseline ADA positive assessment and not fulfilling the conditions of persistently positive.

End point type	Secondary

End point timeframe:

From randomization up to 15 months after first treatment

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Because this is only for combination arms

End point values	Arm A (durvalumab + oleclumab)	Arm B (durvalumab + monalizumab)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	51		
Units: Participants				
ADA positive at any visit (ADA prevalence)	0	1		
Treatment-emergent ADA positive (ADA incidence)	0	1		
Treatment-boosted ADA	0	0		
Treatment-induced ADA	0	1		
ADA positive at baseline only	0	0		
ADA positive post-baseline and at baseline	0	0		
Persistently positive	0	0		
Transiently positive	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and SAEs were collected from time of signature of informed consent up to 12 months post Cycle 1 Day 1. Following the first 12 months post Cycle 1 Day 1, AEs and SAEs were collected up to 3 months post last dose of study treatment.

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs) are defined as events present at baseline that worsen in intensity after administration of study IP or events absent at baseline that emerge after administration of study IP. All TEAEs that occurred on and after first dose up to 90 days after last dose of IP (any) were summarized.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Control Arm (durvalumab monotherapy)

Reporting group description:

Durvalumab 1500 mg IV monotherapy Q4W

Reporting group title	Arm B (durvalumab + monalizumab)

Reporting group description:

Durvalumab 1500 mg IV Q4W + Monalizumab 750 mg IV Q2W

Reporting group title	Arm A (durvalumab + oleclumab)

Reporting group description:

Durvalumab 1500 mg IV Q4W + Oleclumab 3000 mg IV (Q2W for cycles 1 and 2, then Q4W starting cycle 3)

Serious adverse events	Control Arm (durvalumab monotherapy)	Arm B (durvalumab + monalizumab)	Arm A (durvalumab + oleclumab)
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 66 (34.85%)	17 / 61 (27.87%)	20 / 59 (33.90%)
number of deaths (all causes)	27	24	23
number of deaths resulting from adverse events	7	1	4
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Meningioma			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Oesophageal adenocarcinoma			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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

Rectal adenocarcinoma			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Transitional cell carcinoma			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	0 / 66 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyrexia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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
Dyspnoea			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Bronchostenosis			

subjects affected / exposed	0 / 66 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	2 / 66 (3.03%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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
Anoxia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 66 (1.52%)	1 / 61 (1.64%)	0 / 59 (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
Pneumonitis			
subjects affected / exposed	3 / 66 (4.55%)	2 / 61 (3.28%)	6 / 59 (10.17%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 6
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pleural effusion			

subjects affected / exposed	2 / 66 (3.03%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Oesophagobronchial fistula			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Injury, poisoning and procedural complications			
Radiation pneumonitis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	2 / 59 (3.39%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Spinal fracture			
subjects affected / exposed	0 / 66 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 66 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 66 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus arrest			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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

Pericarditis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Pericardial effusion			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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
Acute myocardial infarction			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Pulmonary valve stenosis			
subjects affected / exposed	0 / 66 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 66 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	2 / 66 (3.03%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			

subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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
Eye disorders			
Visual acuity reduced			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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
Renal and urinary disorders			
Glomerulonephritis membranous			
subjects affected / exposed	0 / 66 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Back pain			

subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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
Myopathy			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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
Myositis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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			
Appendicitis			
subjects affected / exposed	0 / 66 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Enterocolitis infectious			
subjects affected / exposed	0 / 66 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected dermal cyst			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Urinary tract infection			
subjects affected / exposed	0 / 66 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord infection			

subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Septic shock			
subjects affected / exposed	0 / 66 (0.00%)	0 / 61 (0.00%)	1 / 59 (1.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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
Pneumonia bacterial			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	5 / 66 (7.58%)	0 / 61 (0.00%)	4 / 59 (6.78%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital infection			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	0 / 59 (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
Metabolism and nutrition disorders			
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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
Hypokalaemia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	0 / 59 (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

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

Non-serious adverse events	Control Arm (durvalumab monotherapy)	Arm B (durvalumab + monalizumab)	Arm A (durvalumab + oleclumab)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 66 (96.97%)	60 / 61 (98.36%)	54 / 59 (91.53%)
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 66 (4.55%)	0 / 61 (0.00%)	3 / 59 (5.08%)
occurrences (all)	4	0	4
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 66 (1.52%)	1 / 61 (1.64%)	3 / 59 (5.08%)
occurrences (all)	1	1	3
Non-cardiac chest pain			
subjects affected / exposed	4 / 66 (6.06%)	5 / 61 (8.20%)	5 / 59 (8.47%)
occurrences (all)	5	5	6
Pyrexia			
subjects affected / exposed	6 / 66 (9.09%)	9 / 61 (14.75%)	7 / 59 (11.86%)
occurrences (all)	8	10	8
Oedema peripheral			
subjects affected / exposed	3 / 66 (4.55%)	5 / 61 (8.20%)	1 / 59 (1.69%)
occurrences (all)	3	5	1
Fatigue			
subjects affected / exposed	7 / 66 (10.61%)	9 / 61 (14.75%)	7 / 59 (11.86%)
occurrences (all)	8	9	8
Asthenia			
subjects affected / exposed	10 / 66 (15.15%)	15 / 61 (24.59%)	11 / 59 (18.64%)
occurrences (all)	11	16	12
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	3 / 66 (4.55%)	1 / 61 (1.64%)	3 / 59 (5.08%)
occurrences (all)	3	2	4
Cough			
subjects affected / exposed	11 / 66 (16.67%)	26 / 61 (42.62%)	19 / 59 (32.20%)
occurrences (all)	12	29	22

Nasal congestion			
subjects affected / exposed	4 / 66 (6.06%)	1 / 61 (1.64%)	0 / 59 (0.00%)
occurrences (all)	4	1	0
Productive cough			
subjects affected / exposed	7 / 66 (10.61%)	5 / 61 (8.20%)	6 / 59 (10.17%)
occurrences (all)	7	6	9
Pneumonitis			
subjects affected / exposed	7 / 66 (10.61%)	8 / 61 (13.11%)	6 / 59 (10.17%)
occurrences (all)	7	8	7
Pleuritic pain			
subjects affected / exposed	1 / 66 (1.52%)	0 / 61 (0.00%)	3 / 59 (5.08%)
occurrences (all)	1	0	3
Pleural effusion			
subjects affected / exposed	2 / 66 (3.03%)	1 / 61 (1.64%)	3 / 59 (5.08%)
occurrences (all)	2	3	3
Dyspnoea			
subjects affected / exposed	17 / 66 (25.76%)	14 / 61 (22.95%)	15 / 59 (25.42%)
occurrences (all)	21	18	20
Dysphonia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 61 (1.64%)	3 / 59 (5.08%)
occurrences (all)	0	1	3
Psychiatric disorders			
Insomnia			
subjects affected / exposed	7 / 66 (10.61%)	5 / 61 (8.20%)	3 / 59 (5.08%)
occurrences (all)	7	5	4
Anxiety			
subjects affected / exposed	0 / 66 (0.00%)	6 / 61 (9.84%)	1 / 59 (1.69%)
occurrences (all)	0	6	1
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	4 / 66 (6.06%)	1 / 61 (1.64%)	8 / 59 (13.56%)
occurrences (all)	7	1	14
Lipase increased			
subjects affected / exposed	6 / 66 (9.09%)	5 / 61 (8.20%)	5 / 59 (8.47%)
occurrences (all)	11	5	6
Amylase increased			

subjects affected / exposed	7 / 66 (10.61%)	5 / 61 (8.20%)	4 / 59 (6.78%)
occurrences (all)	13	7	5
Alanine aminotransferase increased			
subjects affected / exposed	3 / 66 (4.55%)	4 / 61 (6.56%)	3 / 59 (5.08%)
occurrences (all)	3	7	3
Blood creatinine increased			
subjects affected / exposed	4 / 66 (6.06%)	6 / 61 (9.84%)	0 / 59 (0.00%)
occurrences (all)	5	7	0
Injury, poisoning and procedural complications			
Radiation pneumonitis			
subjects affected / exposed	3 / 66 (4.55%)	3 / 61 (4.92%)	5 / 59 (8.47%)
occurrences (all)	3	3	5
Fall			
subjects affected / exposed	5 / 66 (7.58%)	2 / 61 (3.28%)	0 / 59 (0.00%)
occurrences (all)	5	2	0
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	2 / 66 (3.03%)	5 / 61 (8.20%)	1 / 59 (1.69%)
occurrences (all)	2	6	1
Headache			
subjects affected / exposed	2 / 66 (3.03%)	5 / 61 (8.20%)	4 / 59 (6.78%)
occurrences (all)	2	5	5
Hypoaesthesia			
subjects affected / exposed	1 / 66 (1.52%)	4 / 61 (6.56%)	0 / 59 (0.00%)
occurrences (all)	1	4	0
Dizziness			
subjects affected / exposed	0 / 66 (0.00%)	5 / 61 (8.20%)	3 / 59 (5.08%)
occurrences (all)	0	6	4
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 66 (7.58%)	1 / 61 (1.64%)	5 / 59 (8.47%)
occurrences (all)	8	1	9
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 66 (1.52%)	2 / 61 (3.28%)	3 / 59 (5.08%)
occurrences (all)	1	2	3

Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	4 / 66 (6.06%)	1 / 61 (1.64%)	1 / 59 (1.69%)
occurrences (all)	4	1	1
Nausea			
subjects affected / exposed	8 / 66 (12.12%)	5 / 61 (8.20%)	1 / 59 (1.69%)
occurrences (all)	10	7	1
Abdominal pain			
subjects affected / exposed	3 / 66 (4.55%)	2 / 61 (3.28%)	4 / 59 (6.78%)
occurrences (all)	3	2	4
Constipation			
subjects affected / exposed	10 / 66 (15.15%)	2 / 61 (3.28%)	4 / 59 (6.78%)
occurrences (all)	10	2	4
Diarrhoea			
subjects affected / exposed	7 / 66 (10.61%)	13 / 61 (21.31%)	8 / 59 (13.56%)
occurrences (all)	9	19	8
Dry mouth			
subjects affected / exposed	0 / 66 (0.00%)	3 / 61 (4.92%)	3 / 59 (5.08%)
occurrences (all)	0	5	3
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	4 / 66 (6.06%)	4 / 61 (6.56%)	5 / 59 (8.47%)
occurrences (all)	4	5	5
Rash maculo-papular			
subjects affected / exposed	0 / 66 (0.00%)	5 / 61 (8.20%)	2 / 59 (3.39%)
occurrences (all)	0	5	2
Pruritus			
subjects affected / exposed	7 / 66 (10.61%)	15 / 61 (24.59%)	10 / 59 (16.95%)
occurrences (all)	8	18	17
Rash			
subjects affected / exposed	6 / 66 (9.09%)	8 / 61 (13.11%)	9 / 59 (15.25%)
occurrences (all)	7	11	14
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	10 / 66 (15.15%)	13 / 61 (21.31%)	8 / 59 (13.56%)
occurrences (all)	11	14	8
Hyperthyroidism			

subjects affected / exposed	9 / 66 (13.64%)	6 / 61 (9.84%)	7 / 59 (11.86%)
occurrences (all)	10	6	7
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	5 / 66 (7.58%)	5 / 61 (8.20%)	3 / 59 (5.08%)
occurrences (all)	6	6	3
Myalgia			
subjects affected / exposed	3 / 66 (4.55%)	2 / 61 (3.28%)	6 / 59 (10.17%)
occurrences (all)	4	2	7
Back pain			
subjects affected / exposed	6 / 66 (9.09%)	9 / 61 (14.75%)	6 / 59 (10.17%)
occurrences (all)	6	9	6
Arthralgia			
subjects affected / exposed	11 / 66 (16.67%)	11 / 61 (18.03%)	10 / 59 (16.95%)
occurrences (all)	15	14	10
Infections and infestations			
Herpes zoster			
subjects affected / exposed	1 / 66 (1.52%)	4 / 61 (6.56%)	4 / 59 (6.78%)
occurrences (all)	1	4	4
Bronchitis			
subjects affected / exposed	1 / 66 (1.52%)	1 / 61 (1.64%)	4 / 59 (6.78%)
occurrences (all)	1	1	9
Urinary tract infection			
subjects affected / exposed	2 / 66 (3.03%)	1 / 61 (1.64%)	3 / 59 (5.08%)
occurrences (all)	2	1	7
Pneumonia			
subjects affected / exposed	5 / 66 (7.58%)	5 / 61 (8.20%)	1 / 59 (1.69%)
occurrences (all)	7	5	1
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	4 / 66 (6.06%)	1 / 61 (1.64%)	4 / 59 (6.78%)
occurrences (all)	5	1	7
Hyperglycaemia			
subjects affected / exposed	2 / 66 (3.03%)	3 / 61 (4.92%)	6 / 59 (10.17%)
occurrences (all)	2	3	8
Hypercalcaemia			

subjects affected / exposed	3 / 66 (4.55%)	1 / 61 (1.64%)	3 / 59 (5.08%)
occurrences (all)	3	1	4
Decreased appetite			
subjects affected / exposed	6 / 66 (9.09%)	5 / 61 (8.20%)	6 / 59 (10.17%)
occurrences (all)	6	6	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

At data cut-off (18-July-2023), the overall median duration of follow-up was 30.1 months, the overall PFS maturity was 60.8% and the OS maturity was 39.7%. The median OS was not reached in the experimental arms A and B.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/35452273