Clinical trial results:
A Phase IIIB, Single Arm Study, of Durvalumab in Combination with Platinum-Etoposide for Untreated Patients with Extensive-Stage Small Cell Lung Cancer reflecting Real World Clinical Practice in Spain (CANTABRICO).

Summary

EudraCT number	2020-002328-35
Trial protocol	ES
Global end of trial date	21 June 2023

Results information

Result version number	v1
This version publication date	05 July 2024
First version publication date	05 July 2024

Trial information

Trial identification

Sponsor protocol code	D419QC00005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04712903
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Puerto de Somport 21-23, Madrid, Spain, 28050
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +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	12 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 June 2023
Global end of trial reached?	Yes
Global end of trial date	21 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe safety profile of durvalumab in combination with platinum–etoposide as first-line treatment for patients with ES-SCLC

Protection of trial subjects:

The patient signed the informed consent before carrying out any procedure related to the study. Physical examination, hematology, biochemistry, ECG and evaluation of the tumor were made before the inclusion of the patient in the study and during the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 December 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 101
Worldwide total number of subjects	101
EEA total number of subjects	101

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)	44
From 65 to 84 years	57
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Of the 126 patients included in the study, 25 were screening failures and 101 patients have been analysed. All patients included in the analysis started treatment with chemotherapy and durvalumab and 81 of them started maintenance treatment with durvalumab.

Pre-assignment

Screening details:

All patients that met selection critera and sigend the informed consent form were included in the study.

Period 1

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

Arms

Arm title	Experimental arm

Arm description:

Received study intervention

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

Dosage and administration details:

Durvalumab 1500 mgvia IV infusion over 60minutes on Day 1 ofeach cycle.

Number of subjects in period 1	Experimental arm
Started	101
Completed	101

Baseline characteristics

Reporting groups	
Reporting group title	Experimental arm
Reporting group description:	
Received study intervention	

Reporting group values	Experimental arm	Total	
Number of subjects	101	101	
Age Categorical Units: Participants			
<=18 years	0	0	
Between 18 and 65 years	44	44	
>=65 years	57	57	
Age Continuous Units: Years			
arithmetic mean	66.2		
standard deviation	± 7.2	-	
Sex: Female, Male Units:			
Female	33	33	
Male	68	68	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	21	21	
Not Hispanic or Latino	80	80	
Unknown or Not Reported	0	0	
Smoking status Units: Subjects			
Current smoker	46	46	
Former smoker	53	53	
Not available	2	2	
Weight Units: Kg			
arithmetic mean	75.6		
standard deviation	± 16.8	-	

End points

End points reporting groups

Reporting group title	Experimental arm
Reporting group description: Received study intervention	
Subject analysis set title	Completed
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Completed the items in the questionnaire.	
Subject analysis set title	Completed
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Completed the items in the questionnaire.	
Subject analysis set title	Completed
Subject analysis set type	Modified intention-to-treat
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Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Completed the items in the questionnaire.	
Subject analysis set title	Completed
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: Completed the items in the questionnaire.	

Primary: Incidence of adverse events (AEs) grade ≥ 3

End point title	Incidence of adverse events (AEs) grade ≥ 3[1]
End point description: Patients with AEs grade ≥ 3 acording to NCI CTCAE v5.0	
End point type	Primary
End point timeframe: During study treatment	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Single arm, descriptive.

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Participants				
Yes	77			
No	24			

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of immune-mediated adverse events (imAE)

End point title	Incidence of immune-mediated adverse events (imAE)[2]

End point description:

Patients with immune-mediated adverse events (imAE) per patient

End point type	Primary

End point timeframe:

During study treatment

Notes:

[2] - 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: Single arm, descriptive.

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Participants				
Yes	38			
No	63			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)

End point description:

DoR: Defined as the time from the date of first documented response per RECIST1.1 until the first date of documented progression per RECIST1.1 or death in the absence of disease progression.

End point type	Secondary

End point timeframe:

At least every 12 weeks

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: Months				
median (confidence interval 95%)	5.6 (4.7 to 6.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overal Survival (OS)

End point title	Overal Survival (OS)

End point description:

OS: Defined as the time from the first date of treatment until death due to any cause. Any patient not known to have died at the time of analysis will be censored based on the last recorded date on which the patient was known to be alive.

End point type	Secondary

End point timeframe:

Every 12 weeks

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Months				
median (confidence interval 95%)	9.6 (7.8 to 11.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS).

End point title	Progression Free Survival (PFS).

End point description:

PFS: Defined as the time from the first date of treatment until the date of objective disease progression or death (by any cause in the absence of progression) regardless of whether the patient withdraws from investigational product or receives another anticancer therapy prior to progression. Patients who have not progressed or died at the time of analysis will be censored at the time of the latest date of assessment from their last evaluable assessment.

End point type	Secondary

End point timeframe:

At least every 12 weeks

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Months				
median (confidence interval 95%)	6.1 (5.2 to 6.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

Patients who achieve a complete or partial response during study treatment.

End point type	Secondary

End point timeframe:

At least every 12 weeks

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Percentage				
number (confidence interval 95%)	54.5 (44.7 to 64.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Treatment Discontinuation (TTD)

End point title	Time to Treatment Discontinuation (TTD)

End point description:

TTD: Defined as the time from the first date of treatment until the end of treatment date.

End point type	Secondary

End point timeframe:

From start of treatment until end of treatment.

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Months				
median (inter-quartile range (Q1-Q3))	6.2 (4.5 to 9.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: OS rate at 12 months

End point title	OS rate at 12 months

End point description:

Proportion of participants remaining alive at 12 months after initiation of study treatment.

End point type	Secondary

End point timeframe:

Every 12 weeks

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Percentage				
number (confidence interval 95%)	40.7 (31.1 to 50.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: OS rate at 18 months

End point title	OS rate at 18 months

End point description:

Proportion of participants remaining alive at 18 months after initiation of study treatment.

End point type	Secondary

End point timeframe:

Every 12 weeks

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Percentage				
number (confidence interval 95%)	31.6 (22.4 to 40.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS rate at 6 months

End point title	PFS rate at 6 months

End point description:

Proportion of participants remaining alive without disease progression at 6 months after initiation of study treatment.

End point type	Secondary

End point timeframe:

Every 12 weeks

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Percentage				
number (confidence interval 95%)	53.0 (43.2 to 62.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS rate at 12 months

End point title	PFS rate at 12 months

End point description:

Proportion of participants remaining alive without disease progression at 12 months after initiation of study treatment.

End point type	Secondary

End point timeframe:

Every 12 weeks

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Percentage				
number (confidence interval 95%)	21.0 (13.0 to 29.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: DoR rate at 12 months

End point title	DoR rate at 12 months
End point description:	
Proportion of responders remaining alive without disease progression at 12 months after first response.	
End point type	Secondary
End point timeframe:	
Every 12 weeks	

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: Percentage				
number (confidence interval 95%)	35.7 (23.0 to 48.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: OS rate at 6 months

End point title	OS rate at 6 months
End point description:	
Proportion of participants remaining alive at 6 months after initiation of study treatment.	
End point type	Secondary
End point timeframe:	
Every 12 weeks	

End point values	Experimental arm			
Subject group type	Reporting group			
Number of subjects analysed	101			
Units: Percentage				
number (confidence interval 95%)	75.2 (66.8 to 83.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Global Health Status, change from baseline

End point title	QLQ-C30: Global Health Status, change from baseline
End point description:	
Final score minus baseline score	
End point type	Secondary
End point timeframe:	
Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	67			
Units: Units				
arithmetic mean (standard deviation)	-6.3 (± 30.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Role Functioning, change from baseline

End point title	QLQ-C30: Role Functioning, change from baseline
End point description:	
Final score minus baseline score	
End point type	Secondary
End point timeframe:	
Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	69			
Units: Units				
arithmetic mean (standard deviation)	-17.0 (± 36.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Physical Functioning, change from baseline

End point title	QLQ-C30: Physical Functioning, change from baseline

End point description:

Final score minus baseline score

End point type	Secondary

End point timeframe:

Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	69			
Units: Units				
arithmetic mean (standard deviation)	-15.0 (± 29.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Emotional Functioning, change from baseline

End point title	QLQ-C30: Emotional Functioning, change from baseline

End point description:

Final score minus baseline score

End point type	Secondary

End point timeframe:

Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	69			
Units: Units				
arithmetic mean (standard deviation)	-2.3 (± 30.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Cognitive Functioning, change from baseline

End point title	QLQ-C30: Cognitive Functioning, change from baseline
End point description:	
Final score minus baseline score	
End point type	Secondary
End point timeframe:	
Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	69			
Units: Units				
arithmetic mean (standard deviation)	-15.0 (± 24.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Insomnia, change from baseline

End point title	QLQ-C30: Insomnia, change from baseline
End point description:	
Final score minus baseline score	
End point type	Secondary
End point timeframe:	
Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	68			
Units: Units				
arithmetic mean (standard deviation)	1.0 (± 36.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Dyspnea, change from baseline

End point title	QLQ-C30: Dyspnea, change from baseline
End point description:	
Final score minus baseline score	
End point type	Secondary
End point timeframe:	
Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	69			
Units: Units				
arithmetic mean (standard deviation)	-2.4 (± 37.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Nausea, change from baseline

End point title	QLQ-C30: Nausea, change from baseline
End point description:	
Final score minus baseline score	
End point type	Secondary
End point timeframe:	
Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	69			
Units: Units				
arithmetic mean (standard deviation)	0.7 (± 20.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Pain, change from baseline

End point title	QLQ-C30: Pain, change from baseline

End point description:

Final score minus baseline score

End point type	Secondary

End point timeframe:

Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	69			
Units: Units				
arithmetic mean (standard deviation)	0.2 (± 29.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Social Functioning, change from baseline

End point title	QLQ-C30: Social Functioning, change from baseline

End point description:

Final score minus baseline score

End point type	Secondary

End point timeframe:

Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	67			
Units: Units				
arithmetic mean (standard deviation)	-12.0 (± 31.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Fatigue, change from baseline

End point title	QLQ-C30: Fatigue, change from baseline
End point description: Final score minus baseline score	
End point type	Secondary
End point timeframe: Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	69			
Units: Units				
arithmetic mean (standard deviation)	12.4 (± 29.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-LC13: Cough, change from baseline

End point title	QLQ-LC13: Cough, change from baseline
End point description: Final score minus baseline score	
End point type	Secondary
End point timeframe: Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	73			
Units: Units				
arithmetic mean (standard deviation)	-7.8 (± 29.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Diarrhea, change from baseline

End point title	QLQ-C30: Diarrhea, change from baseline

End point description:

Final score minus baseline score

End point type	Secondary

End point timeframe:

Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	69			
Units: Units				
arithmetic mean (standard deviation)	0.0 (± 18.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Financial difficulties, change from baseline

End point title	QLQ-C30: Financial difficulties, change from baseline

End point description:

Final score minus baseline score

End point type	Secondary

End point timeframe:

Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	65			
Units: Units				
arithmetic mean (standard deviation)	10.3 (± 22.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Constipation, change from baseline

End point title	QLQ-C30: Constipation, change from baseline

End point description:

Final score minus baseline score

End point type	Secondary

End point timeframe:

Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	69			
Units: Units				
arithmetic mean (standard deviation)	6.3 (± 33.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-C30: Anorexia, change from baseline

End point title	QLQ-C30: Anorexia, change from baseline

End point description:

Final score minus baseline score

End point type	Secondary

End point timeframe:

Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	69			
Units: Units				
arithmetic mean (standard deviation)	-2.4 (± 36.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-LC13: Haemoptysis, change from baseline

End point title	QLQ-LC13: Haemoptysis, change from baseline

End point description:

Final score minus baseline score

End point type	Secondary

End point timeframe:

Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	73			
Units: Units				
arithmetic mean (standard deviation)	-0.5 (± 15.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-LC13: Pain in arm, change from baseline

End point title	QLQ-LC13: Pain in arm, change from baseline

End point description:

Final score minus baseline score

End point type	Secondary

End point timeframe:

Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	71			
Units: Units				
arithmetic mean (standard deviation)	3.3 (± 33.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-LC13: Sore mouth

End point title	QLQ-LC13: Sore mouth
End point description: Final score minus baseline score	
End point type	Secondary
End point timeframe: Every 3 weeks	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	71			
Units: Units				
arithmetic mean (standard deviation)	2.3 (± 13.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-LC13: Other Pain, change from baseline

End point title	QLQ-LC13: Other Pain, change from baseline
End point description: Final score minus baseline score	
End point type	Secondary
End point timeframe: Every 3 weeks	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	68			
Units: Units				
arithmetic mean (standard deviation)	7.4 (± 39.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-LC13: Dyspnea, change from baseline

End point title	QLQ-LC13: Dyspnea, change from baseline
End point description: Final score minus baseline score	
End point type	Secondary
End point timeframe: Every 3 weeks during chemotherapy treatment and every 4 weeks during maintenance treatment.	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	68			
Units: Units				
arithmetic mean (standard deviation)	3.1 (± 24.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-LC13: Chest pain

End point title	QLQ-LC13: Chest pain
End point description: Final score minus baseline score	
End point type	Secondary
End point timeframe: Every 3 weeks	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	73			
Units: Units				
arithmetic mean (standard error)	-1.8 (± 29.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-LC13: Dysphagia

End point title	QLQ-LC13: Dysphagia
End point description: Final score minus baseline score	
End point type	Secondary
End point timeframe: Every 3 weeks	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	72			
Units: Units				
arithmetic mean (standard error)	2.8 (± 23.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-LC13: Alopecia

End point title	QLQ-LC13: Alopecia
End point description: Final score minus baseline score	
End point type	Secondary
End point timeframe: Every 3 weeks	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	72			
Units: Units				
arithmetic mean (standard deviation)	18.1 (± 37.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: QLQ-LC13: Neuropathy

End point title	QLQ-LC13: Neuropathy
End point description: Final score minus baseline score	
End point type	Secondary
End point timeframe: Every 3 weeks	

End point values	Completed			
Subject group type	Subject analysis set			
Number of subjects analysed	71			
Units: Units				
arithmetic mean (standard deviation)	13.6 (± 27.4)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 18 months	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1
Reporting groups	
Reporting group title	Experimental arm
Reporting group description: Received study intervention	

Serious adverse events	Experimental arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	57 / 101 (56.44%)		
number of deaths (all causes)	76		
number of deaths resulting from adverse events	8		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder neoplasm			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal neoplasm			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Superior vena cava syndrome			
subjects affected / exposed	2 / 101 (1.98%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Peripheral ischaemia			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	5 / 101 (4.95%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 101 (3.96%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Obstructive airways disorder			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	3 / 101 (2.97%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			

subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Transaminases increased			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Radial head dislocation			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac failure			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial flutter			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebellar syndrome			

subjects affected / exposed	1 / 101 (0.99%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	1 / 101 (0.99%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	1 / 101 (0.99%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Immune-mediated neurological disorder				
subjects affected / exposed	1 / 101 (0.99%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Multiple sclerosis				
subjects affected / exposed	1 / 101 (0.99%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neurological decompensation				
subjects affected / exposed	1 / 101 (0.99%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	2 / 101 (1.98%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	1 / 101 (0.99%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				

subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	2 / 101 (1.98%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	2 / 101 (1.98%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	8 / 101 (7.92%)		
occurrences causally related to treatment / all	7 / 10		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	2 / 101 (1.98%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Bile duct stone			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin reaction			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephritis			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal tubular disorder			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	2 / 101 (1.98%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Bone pain			

subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Staphylococcal infection			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	4 / 101 (3.96%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 2		
Respiratory tract infection			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonia			
subjects affected / exposed	6 / 101 (5.94%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	1 / 1		
Herpes zoster reactivation			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	2 / 101 (1.98%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
COVID-19			

subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	3 / 101 (2.97%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Experimental arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 101 (99.01%)		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	15 / 101 (14.85%)		
occurrences (all)	17		
Asthenia			
subjects affected / exposed	64 / 101 (63.37%)		
occurrences (all)	157		
Mucosal inflammation			
subjects affected / exposed	10 / 101 (9.90%)		
occurrences (all)	12		
Oedema peripheral			

subjects affected / exposed	8 / 101 (7.92%)		
occurrences (all)	13		
Illness			
subjects affected / exposed	6 / 101 (5.94%)		
occurrences (all)	8		
Fatigue			
subjects affected / exposed	6 / 101 (5.94%)		
occurrences (all)	10		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	23 / 101 (22.77%)		
occurrences (all)	28		
Dyspnoea			
subjects affected / exposed	31 / 101 (30.69%)		
occurrences (all)	40		
Haemoptysis			
subjects affected / exposed	7 / 101 (6.93%)		
occurrences (all)	7		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 101 (7.92%)		
occurrences (all)	8		
Investigations			
Platelet count decreased			
subjects affected / exposed	11 / 101 (10.89%)		
occurrences (all)	15		
Neutrophil count decreased			
subjects affected / exposed	8 / 101 (7.92%)		
occurrences (all)	15		
Alanine aminotransferase increased			
subjects affected / exposed	7 / 101 (6.93%)		
occurrences (all)	10		
Amylase increased			
subjects affected / exposed	7 / 101 (6.93%)		
occurrences (all)	16		
Lymphocyte count decreased			

subjects affected / exposed	5 / 101 (4.95%)		
occurrences (all)	13		
Gamma-glutamyltransferase increased			
subjects affected / exposed	5 / 101 (4.95%)		
occurrences (all)	11		
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 101 (5.94%)		
occurrences (all)	9		
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 101 (7.92%)		
occurrences (all)	8		
Dysgeusia			
subjects affected / exposed	5 / 101 (4.95%)		
occurrences (all)	6		
Dizziness			
subjects affected / exposed	5 / 101 (4.95%)		
occurrences (all)	6		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	34 / 101 (33.66%)		
occurrences (all)	56		
Anaemia			
subjects affected / exposed	50 / 101 (49.50%)		
occurrences (all)	125		
Thrombocytopenia			
subjects affected / exposed	19 / 101 (18.81%)		
occurrences (all)	27		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	21 / 101 (20.79%)		
occurrences (all)	25		
Constipation			
subjects affected / exposed	27 / 101 (26.73%)		
occurrences (all)	35		
Nausea			

subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	18 / 101 (17.82%) 22 12 / 101 (11.88%) 14		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 24 / 101 (23.76%) 31 12 / 101 (11.88%) 13 8 / 101 (7.92%) 11		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	 6 / 101 (5.94%) 6		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) Hyperthyroidism subjects affected / exposed occurrences (all)	 15 / 101 (14.85%) 19 7 / 101 (6.93%) 8		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	 16 / 101 (15.84%) 19 14 / 101 (13.86%) 23 7 / 101 (6.93%) 7		

Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all) Respiratory tract infection subjects affected / exposed occurrences (all) COVID-19 subjects affected / exposed occurrences (all)	 9 / 101 (8.91%) 11 10 / 101 (9.90%) 12 5 / 101 (4.95%) 5		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hypomagnesaemia subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all) Hyponatraemia subjects affected / exposed occurrences (all)	 18 / 101 (17.82%) 19 10 / 101 (9.90%) 12 9 / 101 (8.91%) 13 9 / 101 (8.91%) 16		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2021	Addition of two biomarker substudies. Additional blood sampling at baseline and every 2 cycles until cycle 8 and a fresh tumor biopsy at disease progression. Updated inclusion criterion 4B in order to allow participation in the study of patients with brain metastases treated with steroids and anticonvulsants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported