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	v2 (current)
This version publication date	02 April 2025
First version publication date	05 July 2024
Version creation reason	

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 signed 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 mg via IV infusion over 60 minutes on Day 1 of each 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.	
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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: Number of patients with adverse events (AEs) grade ≥ 3

End point title	Number of patients with 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, until disease progression (median 6 months)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: 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: Number of patients with immune-mediated adverse events (imAE)

End point title	Number of patients with 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, until disease progression (median 6 months)

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:

From date of randomization until the date of first documented progression or date of death from any cause, whichever came first, assessed up to 2 years

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: 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: 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: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

Per Response Evaluation Criteria In Solid Tumors (RECIST v1.0) Criteria for target lesions: Complete Response (CR), Disappearance of all target lesions; Partial Response (PR), >=30% decrease in the sum of the longest diameter of target lesions; Overall Response (OR) = CR + PR

End point type	Secondary

End point timeframe:

At least every 12 weeks, up to 18 monts

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

End point title	QLQ-C30: Global Health Status, change from baseline

End point description:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For each of these scales, scores range from 0 to 100. For the Global Health Status and the 5 functional

scales a high score indicates better global health status/functioning and a positive change from baseline indicates improvement.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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

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

End point description:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30

is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For each of these scales, scores range from 0 to 100. For the Global Health Status and the 5 functional scales a high score indicates better global health status/functioning and a positive change from baseline indicates improvement.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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: Role Functioning, change from baseline

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

End point description:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For each of these scales, scores range from 0 to 100. For the Global Health Status and the 5 functional scales a high score indicates better global health status/functioning and a positive change from baseline indicates improvement.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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: Insomnia, change from baseline

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

End point description:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For the 9 symptom scales, a high score indicates a higher level of symptoms, and a negative change from Baseline indicates an improvement in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For the 9 symptom scales, a high score indicates a higher level of symptoms, and a negative change from Baseline indicates an improvement in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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: Pain, change from baseline

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

End point description:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For the 9 symptom scales, a high score indicates a higher level of symptoms, and a negative change from Baseline indicates an improvement in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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: Nausea, change from baseline

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

End point description:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For the 9 symptom scales, a high score indicates a higher level of symptoms, and a negative change from Baseline indicates an improvement in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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: Emotional Functioning, change from baseline

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

End point description:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For each of these scales, scores range from 0 to 100. For the Global Health Status and the 5 functional scales a high score indicates better global health status/functioning and a positive change from baseline indicates improvement.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For each of these scales, scores range from 0 to 100. For the Global Health Status and the 5 functional scales a high score indicates better global health status/functioning and a positive change from baseline indicates improvement.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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: Social Functioning, change from baseline

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

End point description:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For each of these scales, scores range from 0 to 100. For the Global Health Status and the 5 functional scales a high score indicates better global health status/functioning and a positive change from baseline indicates improvement.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For the 9 symptom scales, a high score indicates a higher level of symptoms, and a negative change from Baseline indicates an improvement in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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-C30: Diarrhea, change from baseline

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

End point description:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For the 9 symptom scales, a high score indicates a higher level of symptoms, and a negative change from Baseline indicates an improvement in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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: Appetite loss, change from baseline

End point title	QLQ-C30: Appetite loss, change from baseline

End point description:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For the 9 symptom scales, a high score indicates a higher level of symptoms, and a negative change from Baseline indicates an improvement in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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-C30: Constipation, change from baseline

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

End point description:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For the 9 symptom scales, a high score indicates a higher level of symptoms, and a negative change from Baseline indicates an improvement in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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-LC13: Dyspnea, change from baseline

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

End point description:

EORTC QLQ-LC13 is a 13-items questionnaire used in clinical research to assess health-related quality of life in lung cancer patients. The QLQ-LC13 includes questions assessing lung cancer-associated symptoms (Coughing, haemoptysis, dyspnoea and site specific pain), treatment-related side effects (sore mouth, dysphagia, peripheral neuropathy and alopecia) and pain medication.

Scores are calculated and transformed to range from 0 to 100. For the disease symptoms and side-effects of treatment scales a higher score represents a higher level of symptoms/problems and a negative change from baseline value indicates reduction (i.e. improvement) in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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-C30: Financial difficulties, change from baseline

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

End point description:

EORTC QLQ-C30 was administered on day 1 and on the final visit (last treatment visit). EORTC QLQ-C30 is a 30-item questionnaire used to assess the overall quality of life in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical Functioning, Role Functioning, Cognitive Functioning, Emotional Functioning, Social Functioning), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnoea, Insomnia, Appetite Loss, Constipation, Diarrohea, Financial difficulties).

For the 9 symptom scales, a high score indicates a higher level of symptoms, and a negative change from Baseline indicates an improvement in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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-LC13: Cough, change from baseline

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

End point description:

EORTC QLQ-LC13 is a 13-items questionnaire used in clinical research to assess health-related quality of life in lung cancer patients. The QLQ-LC13 includes questions assessing lung cancer-associated symptoms (Coughing, haemoptysis, dyspnoea and site specific pain), treatment-related side effects (sore mouth, dysphagia, peripheral neuropathy and alopecia) and pain medication.

Scores are calculated and transformed to range from 0 to 100. For the disease symptoms and side-effects of treatment scales a higher score represents a higher level of symptoms/problems and a negative change from baseline value indicates reduction (i.e. improvement) in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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-LC13: Haemoptysis, change from baseline

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

End point description:

EORTC QLQ-LC13 is a 13-items questionnaire used in clinical research to assess health-related quality of life in lung cancer patients. The QLQ-LC13 includes questions assessing lung cancer-associated symptoms (Coughing, haemoptysis, dyspnoea and site specific pain), treatment-related side effects (sore mouth, dysphagia, peripheral neuropathy and alopecia) and pain medication.

Scores are calculated and transformed to range from 0 to 100. For the disease symptoms and side-effects of treatment scales a higher score represents a higher level of symptoms/problems and a

negative change from baseline value indicates reduction (i.e. improvement) in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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: Sore mouth

End point title	QLQ-LC13: Sore mouth

End point description:

EORTC QLQ-LC13 is a 13-items questionnaire used in clinical research to assess health-related quality of life in lung cancer patients. The QLQ-LC13 includes questions assessing lung cancer-associated symptoms (Coughing, haemoptysis, dyspnoea and site specific pain), treatment-related side effects (sore mouth, dysphagia, peripheral neuropathy and alopecia) and pain medication.

Scores are calculated and transformed to range from 0 to 100. For the disease symptoms and side-effects of treatment scales a higher score represents a higher level of symptoms/problems and a negative change from baseline value indicates reduction (i.e. improvement) in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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: Neuropathy

End point title	QLQ-LC13: Neuropathy

End point description:

EORTC QLQ-LC13 is a 13-items questionnaire used in clinical research to assess health-related quality of life in lung cancer patients. The QLQ-LC13 includes questions assessing lung cancer-associated symptoms (Coughing, haemoptysis, dyspnoea and site specific pain), treatment-related side effects (sore mouth, dysphagia, peripheral neuropathy and alopecia) and pain medication.

Scores are calculated and transformed to range from 0 to 100. For the disease symptoms and side-effects of treatment scales a higher score represents a higher level of symptoms/problems and a negative change from baseline value indicates reduction (i.e. improvement) in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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

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

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

End point description:

EORTC QLQ-LC13 is a 13-items questionnaire used in clinical research to assess health-related quality of life in lung cancer patients. The QLQ-LC13 includes questions assessing lung cancer-associated symptoms (Coughing, haemoptysis, dyspnoea and site specific pain), treatment-related side effects (sore mouth, dysphagia, peripheral neuropathy and alopecia) and pain medication.

Scores are calculated and transformed to range from 0 to 100. For the disease symptoms and side-effects of treatment scales a higher score represents a higher level of symptoms/problems and a negative change from baseline value indicates reduction (i.e. improvement) in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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: Chest pain

End point title	QLQ-LC13: Chest pain

End point description:

EORTC QLQ-LC13 is a 13-items questionnaire used in clinical research to assess health-related quality of life in lung cancer patients. The QLQ-LC13 includes questions assessing lung cancer-associated symptoms (Coughing, haemoptysis, dyspnoea and site specific pain), treatment-related side effects (sore mouth, dysphagia, peripheral neuropathy and alopecia) and pain medication.

Scores are calculated and transformed to range from 0 to 100. For the disease symptoms and side-effects of treatment scales a higher score represents a higher level of symptoms/problems and a negative change from baseline value indicates reduction (i.e. improvement) in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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:

EORTC QLQ-LC13 is a 13-items questionnaire used in clinical research to assess health-related quality of life in lung cancer patients. The QLQ-LC13 includes questions assessing lung cancer-associated symptoms (Coughing, haemoptysis, dyspnoea and site specific pain), treatment-related side effects (sore mouth, dysphagia, peripheral neuropathy and alopecia) and pain medication.

Scores are calculated and transformed to range from 0 to 100. For the disease symptoms and side-effects of treatment scales a higher score represents a higher level of symptoms/problems and a

negative change from baseline value indicates reduction (i.e. improvement) in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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: Other Pain, change from baseline

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

End point description:

EORTC QLQ-LC13 is a 13-items questionnaire used in clinical research to assess health-related quality of life in lung cancer patients. The QLQ-LC13 includes questions assessing lung cancer-associated symptoms (Coughing, haemoptysis, dyspnoea and site specific pain), treatment-related side effects (sore mouth, dysphagia, peripheral neuropathy and alopecia) and pain medication.

Scores are calculated and transformed to range from 0 to 100. For the disease symptoms and side-effects of treatment scales a higher score represents a higher level of symptoms/problems and a negative change from baseline value indicates reduction (i.e. improvement) in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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: Alopecia

End point title	QLQ-LC13: Alopecia

End point description:

EORTC QLQ-LC13 is a 13-items questionnaire used in clinical research to assess health-related quality of life in lung cancer patients. The QLQ-LC13 includes questions assessing lung cancer-associated symptoms (Coughing, haemoptysis, dyspnoea and site specific pain), treatment-related side effects (sore mouth, dysphagia, peripheral neuropathy and alopecia) and pain medication.

Scores are calculated and transformed to range from 0 to 100. For the disease symptoms and side-effects of treatment scales a higher score represents a higher level of symptoms/problems and a negative change from baseline value indicates reduction (i.e. improvement) in symptoms.

Change from baseline is the difference in the score between the end of treatment visit and the first visit.

End point type	Secondary

End point timeframe:

Baseline (cycle 1 day 1) and end of treatment visit.

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

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)			
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		
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		
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			
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		
Pneumonitis			
subjects affected / exposed	3 / 101 (2.97%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
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		
Haemoptysis			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Dyspnoea			
subjects affected / exposed	4 / 101 (3.96%)		
occurrences causally related to treatment / all	0 / 4		
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			
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		
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		
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			
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			
Dizziness				
subjects affected / exposed	1 / 101 (0.99%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
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			
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			
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			
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		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	2 / 101 (1.98%)		
occurrences causally related to treatment / all	1 / 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		
Pancytopenia			
subjects affected / exposed	2 / 101 (1.98%)		
occurrences causally related to treatment / all	3 / 3		
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			
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		
Vomiting			
subjects affected / exposed	2 / 101 (1.98%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

Hepatobiliary disorders			
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		
Hepatitis			
subjects affected / exposed	1 / 101 (0.99%)		
occurrences causally related to treatment / all	1 / 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				
Bronchitis				
subjects affected / exposed	1 / 101 (0.99%)			
occurrences causally related to treatment / all	0 / 1			
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			
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			
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			
Pneumonia				
subjects affected / exposed	6 / 101 (5.94%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	1 / 1			
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			
Sepsis				
subjects affected / exposed	4 / 101 (3.96%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 2			
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		
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		
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			
Asthenia			
subjects affected / exposed	64 / 101 (63.37%)		
occurrences (all)	157		
Pyrexia			
subjects affected / exposed	15 / 101 (14.85%)		
occurrences (all)	17		
Oedema peripheral			
subjects affected / exposed	8 / 101 (7.92%)		
occurrences (all)	13		
Fatigue			

subjects affected / exposed	6 / 101 (5.94%)		
occurrences (all)	10		
Illness			
subjects affected / exposed	6 / 101 (5.94%)		
occurrences (all)	8		
Mucosal inflammation			
subjects affected / exposed	10 / 101 (9.90%)		
occurrences (all)	12		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	31 / 101 (30.69%)		
occurrences (all)	40		
Cough			
subjects affected / exposed	23 / 101 (22.77%)		
occurrences (all)	28		
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			
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		
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 101 (5.94%)		
occurrences (all)	9		
Gamma-glutamyltransferase			

increased			
subjects affected / exposed	5 / 101 (4.95%)		
occurrences (all)	11		
Lymphocyte count decreased			
subjects affected / exposed	5 / 101 (4.95%)		
occurrences (all)	13		
Platelet count decreased			
subjects affected / exposed	11 / 101 (10.89%)		
occurrences (all)	15		
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 101 (7.92%)		
occurrences (all)	8		
Dizziness			
subjects affected / exposed	5 / 101 (4.95%)		
occurrences (all)	6		
Dysgeusia			
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		
Thrombocytopenia			
subjects affected / exposed	19 / 101 (18.81%)		
occurrences (all)	27		
Anaemia			
subjects affected / exposed	50 / 101 (49.50%)		
occurrences (all)	125		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	27 / 101 (26.73%)		
occurrences (all)	35		
Diarrhoea			
subjects affected / exposed	21 / 101 (20.79%)		
occurrences (all)	25		
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) Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 24 / 101 (23.76%) 31 8 / 101 (7.92%) 11 12 / 101 (11.88%) 13		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	 6 / 101 (5.94%) 6		
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all) Hypothyroidism subjects affected / exposed occurrences (all)	 7 / 101 (6.93%) 8 15 / 101 (14.85%) 19		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 7 / 101 (6.93%) 7 14 / 101 (13.86%) 23 16 / 101 (15.84%) 19		

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

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