Clinical trial results:
A Phase IIIb, Single Arm Study of Carboplatin or Cisplatin Plus Etoposide with Atezolizumab (Anti-PD-L1 Antibody) in Patients with Untreated Extensive-Stage Small Cell Lung Cancer

Summary

EudraCT number	2019-002784-10
Trial protocol	ES
Global end of trial date	14 December 2022

Results information

Result version number	v1 (current)
This version publication date	14 December 2023
First version publication date	14 December 2023

Trial information

Trial identification

Sponsor protocol code	ML41599

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Roche Farma S.A. (Soc. Unipersonal)
Sponsor organisation address	C/Ribera del Lora 50, Madrid, Spain, 28042
Public contact	Roche Farma S.A. (Soc. Unipersonal), Roche Farma S.A. (Soc. Unipersonal), 34 913253700, spain.start_up_unit@roche.com
Scientific contact	Roche Farma S.A. (Soc. Unipersonal), Roche Farma S.A. (Soc. Unipersonal), 34 913253700, spain.start_up_unit@roche.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	14 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study is being conducted to evaluate the safety of atezolizumab + carboplatin or cisplatin + etoposide as first-line treatment for extensive-stage small cell lung cancer.

Protection of trial subjects:

All study subjects were required to read and sign and Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 December 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 155
Worldwide total number of subjects	155
EEA total number of subjects	155

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)	73
From 65 to 84 years	81
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 29 centers in one country.

Pre-assignment

Screening details:

A total of 155 participants were enrolled at 29 centers.

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	Atezolizumab + Cisplatin/Carboplatin + Etoposide

Arm description:

Participants will receive the following treatment regimen: atezolizumab + cisplatin/carboplatin + etoposide. Induction treatment will be administered on a 21-day cycle for four or six cycles (according to investigator's choice). Following the induction phase, participants will continue maintenance therapy with atezolizumab. Participants will be treated until loss of clinical benefit, or unaccepted toxicity, or withdrawal of consent, or death (whichever occurs first).

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

Dosage and administration details:

Atezolizumab will be administered by intravenous infusion at a fixed dose of 1200 mg on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator.

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

Dosage and administration details:

Carboplatin will be administered as intravenous infusion at a dose of area under the concentration-time curve (AUC) of 5 mg/mL/min on Day 1 of each 21-day cycle during the induction phase (Cycles 1-4).

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

Dosage and administration details:

Etoposide will be administered intravenously at a dose of 100 mg/m^2 on Days 1, 2 and 3 of each 21-day cycle during the induction phase (Cycles 1-4).

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

Dosage and administration details:

Cisplatin will be administered as intravenous infusion at a dose of 75 mg per meter squared (75 mg/m^2) after completion of atezolizumab on Day 1 of each 21-day cycle during the induction phase (Cycles 1-4).

Number of subjects in period 1	Atezolizumab + Cisplatin/Carboplatin + Etoposide
Started	155
Completed	0
Not completed	155
Death	128
Withdrawal by Subject	1
Study Terminated by Sponsor	22
Lost to follow-up	4

Baseline characteristics

Reporting groups	
Reporting group title	Atezolizumab + Cisplatin/Carboplatin + Etoposide
Reporting group description:	
Participants will receive the following treatment regimen: atezolizumab + cisplatin/carboplatin + etoposide. Induction treatment will be administered on a 21-day cycle for four or six cycles (according to investigator's choice). Following the induction phase, participants will continue maintenance therapy with atezolizumab. Participants will be treated until loss of clinical benefit, or unaccepted toxicity, or withdrawal of consent, or death (whichever occurs first).	

Reporting group values	Atezolizumab + Cisplatin/Carboplatin + Etoposide	Total	
Number of subjects	155	155	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	73	73	
From 65-84 years	81	81	
85 years and over	1	1	
Age continuous Units: years			
arithmetic mean	64.67		
standard deviation	± 8.87	-	
Gender categorical Units: Subjects			
Female	43	43	
Male	112	112	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	14	14	
Not Hispanic or Latino	140	140	
Not Reported	1	1	
Unknown	0	0	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Black or African American	0	0	
Native Hawaiian or Pacific Islander	0	0	
White	154	154	
Unknown	1	1	

End points

End points reporting groups

Reporting group title	Atezolizumab + Cisplatin/Carboplatin + Etoposide

Reporting group description:

Participants will receive the following treatment regimen: atezolizumab + cisplatin/carboplatin + etoposide. Induction treatment will be administered on a 21-day cycle for four or six cycles (according to investigator's choice). Following the induction phase, participants will continue maintenance therapy with atezolizumab. Participants will be treated until loss of clinical benefit, or unaccepted toxicity, or withdrawal of consent, or death (whichever occurs first).

Primary: Mean Number of Cycles of Carboplatin or Cisplatin

End point title	Mean Number of Cycles of Carboplatin or Cisplatin[1]

End point description:

There is 4 or 6 cycles of carboplatin or cisplatin. Each cycle is 21 days. A participant can have cycles of carboplatin and cisplatin during induction phase.

End point type	Primary

End point timeframe:

From Baseline up to 18 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Cycle				
arithmetic mean (standard deviation)	4.49 (± 1.40)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Number of Cycles of Atezolizumab (Both Induction and Maintenance Phases)

End point title	Mean Number of Cycles of Atezolizumab (Both Induction and Maintenance Phases)[2]

End point description:

The induction phase of the study will consist of four or six cycles of atezolizumab plus chemotherapy, with each cycle being 21 days in duration. After the induction phase, patients will begin maintenance therapy with atezolizumab every 3 weeks.

End point type	Primary

End point timeframe:

Baseline up to 36 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carbo platin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Cycles				
arithmetic mean (standard deviation)	11.39 (± 9.47)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Treatment Duration of Atezolizumab

End point title	Mean Treatment Duration of Atezolizumab[3]

End point description:

Treatment duration is defined as the total number of days from first treatment administration to the last treatment administration +1.

End point type	Primary

End point timeframe:

Baseline up to approximately 36 months

Notes:

[3] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carbo platin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Days				
arithmetic mean (standard deviation)	242.10 (± 214.66)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Dose Interruption

End point title	Percentage of Participants with Dose Interruption[4]

End point description:

End point type	Primary

End point timeframe:

From baseline up to 36 months

Notes:

[4] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: percentage of participants				
number (not applicable)				
Yes	78.06			
No	21.94			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Number of Cycles of Etoposide

End point title	Mean Number of Cycles of Etoposide[5]

End point description:

There is 4 or 6 cycles of etoposide. Each cycle is 21 days.

End point type	Primary

End point timeframe:

From baseline up to 18 months

Notes:

[5] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Cycle				
arithmetic mean (standard deviation)	4.57 (± 1.35)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Transient or Permanent Dose Interruption

End point title	Percentage of Participants with Transient or Permanent Dose

	Interruption[6]

End point description:

A participant can be counted in several categories.

End point type	Primary

End point timeframe:

From baseline to 36 months

Notes:

[6] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	121			
Units: Percentage of Participants				
number (not applicable)				
Transient	91.74			
Permanent	21.49			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Receiving Cycles of Chemotherapy

End point title	Percentage of Participants Receiving Cycles of Chemotherapy[7]

End point description:

The cycles range from less than 4 cycles to 6 cycles. Each cycle is 21 days.

End point type	Primary

End point timeframe:

From Baseline to 18 months

Notes:

[7] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Percentage of Participants				
number (not applicable)				
Less than 4 cycles	9.68			
4 cycles	49.03			
5 cycles	2.58			
6 cycles	38.71			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Treatment Emergent AEs Leading to Study Drug Discontinuation or Interruption by Primary System Organ Class

End point title	Percentage of Participants with Treatment Emergent AEs Leading to Study Drug Discontinuation or Interruption by Primary System Organ Class[8]

End point description:

Treatment-emergent AE (TEAE) is defined as an AE that began after the start of trial medication treatment. The dictionary used was MedDRA v25.1

End point type	Primary

End point timeframe:

From baseline up to 36 months

Notes:

[8] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Percentage of Participants				
number (not applicable)				
Any Class	76.77			
Blood and Lymphatic System Disorders	34.19			
Investigations	21.29			
General Disorders and Admin Site Conditions	14.84			
Infections and Infestations	14.84			
Gastrointestinal Disorders	13.55			
Respiratory, Thoracic and Mediastinal Disorders	9.03			
Nervous System Disorders	7.10			
Metabolism and Nutrition Disorders	6.45			
Endocrine Disorders	4.52			
Renal and Urinary Disorders	3.87			
Musculoskeletal and Connective Tissue Disorders	3.23			
Psychiatric Disorders	3.23			
Skin and Subcutaneous Tissue Disorders	2.58			
Cardiac Disorders	1.94			
Vascular Disorders	1.94			
Eye Disorders	0.65			

Hepatobiliary Disorders	0.65			
Neoplasms Benign, Malignant and Unspecified	0.65			
Social Circumstances	0.65			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Taking Concomitant Medications (Corticosteroids) by Anatomic Class

End point title	Percentage of Participants Taking Concomitant Medications (Corticosteroids) by Anatomic Class[9]

End point description:

Concomitant therapy includes any medication used by a patient from 7 days prior to screening until the treatment discontinuation visit. Participants with premedication are included in the table. A medication can be counted in several categories.

End point type	Primary

End point timeframe:

From baseline up to 36 months

Notes:

[9] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Percentage of Participants				
number (not applicable)				
Any Concomitant Medications	91.61			
Systemic Hormonal Preparations	88.39			
Dermatologicals	14.84			
Respiratory System	10.32			
Alimentary Tract and Metabolism	1.29			
Blood and Blood Forming Organs	0.65			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Taking Concomitant Medications by Anatomic Class

End point title	Percentage of Participants Taking Concomitant Medications by Anatomic Class[10]

End point description:

Concomitant therapy includes any medication used by a patient from 7 days prior to screening until the

treatment discontinuation visit. Participants with premedication are included in the table. A medication can be counted in several categories.

End point type	Primary

End point timeframe:

From baseline up to 36 months

Notes:

[10] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Percentage of Participants				
number (not applicable)				
Any Concomitant Medications	100			
Alimentary Tract and Metabolism	97.42			
Systemic Hormonal Preparations	90.32			
Nervous System	86.45			
Blood and Blood Forming Organs	67.10			
Antineoplastic and Immunomodulating Agents	59.35			
Antiinfectives for Systemic Use	58.06			
Cardiovascular System	54.84			
Respiratory System	45.16			
Musculo-Skeletal System	41.94			
Dermatologicals	20.65			
Genito Urinary System & Sex Hormones	10.97			
Sensory Organs	7.74			
Various	7.74			

Statistical analyses

No statistical analyses for this end point

Primary: Kaplan-Meier Cumulative Incidence Probability of Treatment Emergent AEs of Special Interest During Treatment Period

End point title	Kaplan-Meier Cumulative Incidence Probability of Treatment Emergent AEs of Special Interest During Treatment Period[11]

End point description:

Out of 155 participants, 148 participants were censored and there were 7 events. Event is any patient who has experienced at least one treatment emergent AE of special interest during treatment period. Censor is any patient who has not experienced a treatment emergent AE of special interest during treatment period.

End point type	Primary

End point timeframe:

From baseline to 36 months

Notes:

[11] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: percentage				
number (confidence interval 95%)				
At 200 days	1.58 (0.40 to 6.15)			
At 400 days	6.01 (2.00 to 17.33)			
At 600 days	16.45 (6.40 to 38.64)			
At 800 days	23.41 (10.00 to 49.10)			
At 1000 days	23.41 (10.00 to 49.10)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Treatment Emergent AEs

End point title	Percentage of Participants with Treatment Emergent AEs[12]

End point description:

Percentage of participants with at least one treatment AE. Clopper-Pearson is used for 95% confidence interval.

End point type	Primary

End point timeframe:

From baseline up to 36 months

Notes:

[12] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: percentage of participants				
number (confidence interval 95%)				
Any Grade	100 (97.6 to 100)			
Grade 1-2	98.1 (94.4 to 99.6)			
Grade 3-4	72.3 (64.5 to 79.1)			

Grade 5	11.6 (7.0 to 17.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Treatment Related AEs

End point title	Percentage of Participants with Treatment Related AEs[13]

End point description:

Percentage of participants with at least one treatment emergent AE. Clopper-Pearson is used for 95% confidence interval.

End point type	Primary

End point timeframe:

From baseline up to 36 months

Notes:

[13] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: percentage of participants				
number (confidence interval 95%)				
Any Grade	74.2 (66.6 to 80.9)			
Grade 1-2	68.4 (60.4 to 75.6)			
Grade 3-4	27.7 (20.9 to 35.5)			
Grade 5	0.6 (0.0 to 3.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Treatment Related SAEs

End point title	Percentage of Participants with Treatment Related SAEs[14]

End point description:

Percentage of participants with at least one treatment emergent AE. Clopper-Pearson is used for 95% confidence interval.

End point type	Primary

End point timeframe:

From baseline up to 36 months

Notes:

[14] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: percentage of participants				
number (confidence interval 95%)				
Any Grade	12.3 (7.5 to 18.5)			
Grade 1-2	1.9 (0.4 to 5.6)			
Grade 3-4	10.3 (6.0 to 16.2)			
Grade 5	0.6 (0.0 to 3.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change in Diastolic Blood Pressure

End point title	Mean Change in Diastolic Blood Pressure[15]

End point description:

The mean changes are recorded at baseline, during and following study treatment administration.

End point type	Primary

End point timeframe:

Baseline, Induction Phase(IP) Cycle(C) 1 pre- & post-dose, IPC2 pre- & post-dose, IPC3 pre- & post-dose, IPC4 pre- & post-dose, Maintenance Phase(MP) Visit(V) 1 pre- & post-dose, MPV2 pre- & post-dose, MPV3 pre- & post-dose, MPV4 pre- & post-dose

Notes:

[15] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: mm Hg				
arithmetic mean (standard deviation)				
Baseline (n=155)	75.17 (± 11.09)			
IP Cycle 1 pre-dose (n=143)	0.00 (± 0.00)			
IP Cycle 1 post dose (n=93)	-0.59 (± 8.96)			
IP Cycle 2 pre-dose (n=144)	-3.22 (± 9.79)			
IP Cycle 2 post-dose (n=72)	-2.61 (± 10.36)			

IP Cycle 3 pre-dose (n=140)	-2.76 (± 10.29)			
IP Cycle 3 post-dose (n=69)	-3.38 (± 9.16)			
IP Cycle 4 pre-dose (n=134)	-2.85 (± 10.72)			
IP Cycle 4 post-dose (n=58)	-2.28 (± 9.73)			
MP Visit 1 pre-dose (n=124)	-2.15 (± 10.90)			
MP Visit 1 post-dose (n=55)	-1.04 (± 11.61)			
MP Visit 2 pre-dose (n=112)	-1.35 (± 10.53)			
MP Visit 2 post-dose (n=49)	-1.84 (± 12.26)			
MP Visit 3 pre-dose (n=91)	-1.00 (± 10.77)			
MP Visit 3 post-dose (n=44)	0.25 (± 9.32)			
MP Visit 4 pre-dose (n=74)	-1.59 (± 11.14)			
MP Visit 4 post-dose (n=35)	1.83 (± 10.67)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Treatment Emergent AEs of Special Interest

End point title	Percentage of Participants with Treatment Emergent AEs of Special Interest[16]

End point description:

Percentage of participants with at least one treatment emergent AE of special interest. Clopper-Pearson is used for 95% confidence interval.

End point type	Primary

End point timeframe:

from baseline up to 36 months

Notes:

[16] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: percentage of participants				
number (confidence interval 95%)				
Any Grade	4.5 (1.8 to 9.1)			
Grade 1-2	2.6 (0.7 to 6.5)			
Grade 3-4	1.3 (0.2 to 4.6)			
Grade 5	0.6 (0.0 to 3.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change in Systolic Blood Pressure

End point title	Mean Change in Systolic Blood Pressure[17]

End point description:

The mean changes are recorded at baseline, during and following study treatment administration.

End point type	Primary

End point timeframe:

Baseline, IPC1 pre- & post-dose, IPC2 pre- & post-dose, IPC3 pre- & post-dose, IPC4 pre- & post-dose, MPV1 pre- & post-dose, MPV2 pre- & post-dose, MPV3 pre- & post-dose, MPV4 pre- & post-dose

Notes:

[17] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: mm Hg				
arithmetic mean (standard deviation)				
Baseline	126.10 (± 17.03)			
IP Cycle 1 pre-dose (n=143)	0.00 (± 0.00)			
IP Cycle 1 post-dose (n=93)	1.24 (± 14.97)			
IP Cycle 2 pre-dose (n=144)	-4.69 (± 16.94)			
IP Cycle 2 post-dose (n=72)	-2.64 (± 16.16)			
IP Cycle 3 pre-dose (n=140)	-4.16 (± 16.89)			
IP Cycle 3 post-dose (n=69)	-2.35 (± 14.67)			
IP Cycle 4 pre-dose (n=134)	-3.12 (± 18.82)			
IP Cycle 4 post-dose (n=58)	0.00 (± 15.69)			
MP Visit 1 pre-dose (n=124)	-2.98 (± 20.00)			
MP Visit 1 post-dose (n=55)	1.04 (± 19.98)			
MP Visit 2 pre-dose (n=112)	-0.57 (± 23.17)			
MP Visit 2 post-dose (n=49)	-0.55 (± 23.17)			
MP Visit 3 pre-dose (n=91)	-1.07 (± 18.51)			
MP Visit 3 post-dose (n=44)	0.34 (± 15.07)			

MP Visit 4 pre-dose (n=74)	-0.81 (± 20.19)			
MP Visit 4 post-dose (n=35)	0.31 (± 18.47)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change in Weight

End point title	Mean Change in Weight[18]

End point description:

The mean changes are recorded at baseline, during and following study treatment administration.

End point type	Primary

End point timeframe:

Baseline, IPC1 pre- & post-dose, IPC2 pre- & post-dose, IPC3 pre- & post-dose, IPC4 pre- & post-dose, MPV1 pre- & post-dose, MPV2 pre- & post-dose, MPV3 pre- & post-dose, MPV4 pre- & post-dose

Notes:

[18] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: kg				
arithmetic mean (standard deviation)				
Baseline (n=153)	73.81 (± 14.82)			
IP Cycle 1 pre dose (n=130)	0.00 (± 0.00)			
IP Cycle 1 post-dose (n=67)	-0.02 (± 0.13)			
IP Cycle 2 pre dose (n=135)	-0.11 (± 4.15)			
IP Cycle 2 post-dose (n=59)	-0.52 (± 3.42)			
IP Cycle 3 pre dose (n=134)	-0.37 (± 3.34)			
IP Cycle 3 post-dose (n=58)	-0.20 (± 4.05)			
IP Cycle 4 pre dose (n=131)	0.21 (± 4.11)			
IP Cycle 4 post-dose (n=51)	0.33 (± 4.32)			
MP Visit 1 pre-dose (n=122)	1.17 (± 4.95)			
MP Visit 1 post-dose (n=46)	0.52 (± 4.42)			
MP Visit 2 pre-dose (n=111)	1.41 (± 5.62)			
MP Visit 2 post-dose (n=38)	0.89 (± 5.26)			
MP Visit 3 pre-dose (n=90)	2.17 (± 5.94)			
MP Visit 3 post-dose (n=36)	1.18 (± 6.73)			
MP Visit 4 pre-dose (n=74)	3.13 (± 6.05)			
MP Visit 4 post-dose (n=28)	1.19 (± 5.09)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change in Pulse Rate

End point title	Mean Change in Pulse Rate[19]

End point description:

The mean changes are recorded at baseline, during and following study treatment administration.

End point type	Primary

End point timeframe:

Baseline, IPC1 pre- & post-dose, IPC2 pre- & post-dose, IPC3 pre- & post-dose, IPC4 pre- & post-dose, MPV1 pre- & post-dose, MPV2 pre- & post-dose, MPV3 pre- & post-dose, MPV4 pre- & post-dose

Notes:

[19] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: beats/min				
arithmetic mean (standard deviation)				
Baseline (n=155)	84.12 (± 14.49)			
IP Cycle 1 pre-dose (n=143)	0.00 (± 0.00)			
IP Cycle 1 post-dose (n=93)	-3.08 (± 11.89)			
IP Cycle 2 pre-dose (n=144)	-2.55 (± 14.56)			
IP Cycle 2 post-dose (n=72)	-3.63 (± 16.06)			
IP Cycle 3 pre-dose (n=140)	-1.73 (± 13.87)			
IP Cycle 3 post-dose (n=69)	-4.07 (± 13.26)			
IP Cycle 4 pre-dose (n=134)	-3.14 (± 14.40)			
IP Cycle 4 post-dose (n=58)	-5.03 (± 14.64)			
MP Visit 1 pre-dose (n=124)	-1.77 (± 14.34)			
MP Visit 1 post-dose (n=55)	-3.38 (± 12.90)			
MP Visit 2 pre-dose (n=112)	-3.33 (± 13.04)			
MP Visit 2 post-dose (n=47)	-4.91 (± 14.11)			
MP Visit 3 pre-dose (n=91)	-2.46 (± 14.37)			
MP Visit 3 post-dose (n=44)	-4.16 (± 15.44)			
MP Visit 4 pre-dose (n=74)	-3.72 (± 13.94)			
MP Visit 4 post-dose (n=34)	-5.65 (± 16.11)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change in Respiratory Rate

End point title	Mean Change in Respiratory Rate[20]

End point description:

The mean changes are recorded at baseline, during and following study treatment administration.

End point type	Primary

End point timeframe:

Baseline, IPC1 pre- & post-dose, IPC2 pre- & post-dose, IPC3 pre- & post-dose, IPC4 pre- & post-dose, MPV1 pre- & post-dose, MPV2 pre- & post-dose, MPV3 pre- & post-dose, MPV4 pre- & post-dose

Notes:

[20] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: breaths/min				
arithmetic mean (standard deviation)				
Baseline (n=149)	17.04 (± 2.62)			
IP Cycle 1 pre-dose (n=134)	0.00 (± 0.00)			
IP Cycle 1 post-dose (n=90)	-0.37 (± 1.80)			
IP Cycle 2 pre-dose (n=136)	-0.25 (± 2.49)			
IP Cycle 2 post-dose (n=72)	-0.04 (± 2.17)			
IP Cycle 3 pre-dose (n=131)	-0.56 (± 2.58)			
IP Cycle 3 post-dose (n=68)	-0.47 (± 2.47)			
IP Cycle 4 pre-dose (n=123)	-0.52 (± 2.51)			
IP Cycle 4 post-dose (n=58)	-0.29 (± 2.23)			
MP Visit 1 pre-dose (n=114)	-0.31 (± 2.60)			
MP Visit 1 post-dose (n=55)	0.11 (± 2.07)			
MP Visit 2 pre-dose (n=103)	-0.21 (± 2.49)			
MP Visit 2 post-dose (n=47)	-0.38 (± 2.13)			
MP Visit 3 pre-dose (n=88)	-0.33 (± 2.21)			
MP Visit 3 post-dose (n=43)	-0.14 (± 2.10)			
MP Visit 4 pre-dose (n=72)	0.00 (± 2.05)			
MP Visit 4 post-dose (n=33)	-0.12 (± 1.19)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change in Lymphocytes

End point title	Mean Change in Lymphocytes[21]

End point description:

The mean changes are recorded at baseline, during and following study treatment administration.

End point type	Primary

End point timeframe:

Baseline, IP Cycle 2, IP Cycle 3, IP Cycle 4, MP Visit 1, MP Visit 2, MP Visit 3, MP Visit 4

Notes:

[21] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: 10^9/L				
arithmetic mean (standard deviation)				
Baseline (n=155)	1.62 (± 0.70)			
IP Cycle 2 (n=145)	0.37 (± 1.81)			
IP Cycle 3 (n=139)	0.25 (± 0.93)			
IP Cycle 4 (n=139)	0.14 (± 0.82)			
MP Cycle 1 (n=131)	0.24 (± 3.57)			
MP Cycle 2 (n=117)	-0.03 (± 0.76)			
MP Cycle 3 (n=97)	-0.07 (± 0.86)			
MP Cycle 4 (n=78)	-0.02 (± 0.94)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change in Neutrophils

End point title	Mean Change in Neutrophils[22]

End point description:

The mean changes are recorded at baseline, during and following study treatment administration.

End point type	Primary

End point timeframe:

Baseline, IP Cycle 2, IP Cycle 3, IP Cycle 4, MP Visit 1, MP Visit 2, MP Visit 3, MP Visit 4

Notes:

[22] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: 10^9/L				
arithmetic mean (standard deviation)				
Baseline (n=155)	7.26 (± 5.96)			
IP Cycle 2 (n=144)	-1.94 (± 6.99)			
IP Cycle 3 (n=139)	-2.74 (± 6.51)			
IP Cycle 4 (n=139)	-2.94 (± 7.53)			
MP Cycle 1 (n=130)	-3.02 (± 9.11)			
MP Cycle 2 (n=117)	-2.35 (± 6.67)			
MP Cycle 3 (n=97)	-2.78 (± 6.93)			
MP Cycle 4 (=78)	-2.88 (± 7.92)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change in Platelets

End point title	Mean Change in Platelets[23]

End point description:

The mean changes are recorded at baseline, during and following study treatment administration.

End point type	Primary

End point timeframe:

Baseline, IP Cycle 2, IP Cycle 3, IP Cycle 4, MP Visit 1, MP Visit 2, MP Visit 3, MP Visit 4

Notes:

[23] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: 10^9/L				
arithmetic mean (standard deviation)				
Baseline (n=155)	281.86 (± 97.99)			
IP Cycle 2 (n=149)	75.67 (± 139.58)			
IP Cycle 3 (n=142)	41.92 (± 138.54)			
IP Cycle 4 (n=140)	1.07 (± 117.87)			
MP Cycle 1 (n=133)	-48.47 (± 108.75)			
MP Cycle 2 (n=117)	-57.80 (± 78.91)			

MP Cycle 3 (n=97)	-70.39 (± 81.19)			
MP Cycle 4 (n=78)	-61.44 (± 89.35)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change in Neutrophil-to-Lymphocyte Ratio

End point title	Mean Change in Neutrophil-to-Lymphocyte Ratio[24]

End point description:

The mean changes are recorded at baseline, during and following study treatment administration.

End point type	Primary

End point timeframe:

Baseline, IP Cycle 2, IP Cycle 3, IP Cycle 4, MP Visit 1, MP Visit 2, MP Visit 3, MP Visit 4

Notes:

[24] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: not applicable				
arithmetic mean (standard deviation)				
Baseline (n=155)	5.40 (± 5.09)			
IP Cycle 2 (n=144)	-1.73 (± 5.33)			
IP Cycle 3 (n=139)	-2.30 (± 4.49)			
IP Cycle 4 (n=139)	-2.31 (± 5.10)			
MP Cycle 1 (n=130)	-2.00 (± 6.36)			
MP Cycle 2 (n=117)	-1.15 (± 5.04)			
MP Cycle 3 (n=97)	-1.42 (± 4.48)			
MP Cycle 4 (n=78)	-1.18 (± 5.86)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change in Platelet-to-Lymphocyte Ratio

End point title	Mean Change in Platelet-to-Lymphocyte Ratio[25]

End point description:

The mean changes are recorded at baseline, during and following study treatment administration.

End point type	Primary

End point timeframe:

Baseline, IP Cycle 2, IP Cycle 3, IP Cycle 4, MP Visit 1, MP Visit 2, MP Visit 3, MP Visit 4

Notes:

[25] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: not applicable				
arithmetic mean (standard deviation)				
Baseline (n=155)	206.94 (± 123.36)			
IP Cycle 2 (n=145)	22.14 (± 154.59)			
IP Cycle 3 (n=139)	-2.92 (± 132.91)			
IP Cycle 4 (n=139)	-17.92 (± 121.78)			
MP Cycle 1 (n=131)	-24.28 (± 128.33)			
MP Cycle 2 (n=117)	-30.32 (± 112.68)			
MP Cycle 3 (n=97)	-36.59 (± 104.34)			
MP Cycle 4 (n=78)	-27.38 (± 112.91)			

Statistical analyses

No statistical analyses for this end point

Primary: Mean Change to Lactate Dehydrogenase

End point title	Mean Change to Lactate Dehydrogenase[26]

End point description:

The mean changes are recorded at baseline, during and following study treatment administration.

End point type	Primary

End point timeframe:

Baseline, IP Cycle 2, IP Cycle 3, IP Cycle 4, MP Visit 1, MP Visit 2, MP Visit 3, MP Visit 4

Notes:

[26] - 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: There was no statistical analysis done for the outcome measure.

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: IU/L				
arithmetic mean (standard deviation)				
Baseline (n=150)	397.31 (± 402.77)			
IP Cycle 2 (n=133)	-125.63 (± 331.98)			
IP Cycle 3 (n=127)	-139.38 (± 355.03)			
IP Cycle 4 (n=131)	-138.41 (± 357.07)			
MP Cycle 1 (n=121)	-109.66 (± 338.68)			
MP Cycle 2 (n=103)	-87.79 (± 226.60)			
MP Cycle 3 (n=85)	-53.56 (± 307.61)			
MP Cycle 4 (n=68)	-84.56 (± 196.65)			

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 initiation of study treatment to the first occurrence of disease progression or death from any cause (whichever occurs first), as determined by the investigator according to RECIST v1.1.

End point type	Secondary

End point timeframe:

Baseline to the first occurrence of disease progression or death from any cause (whichever occurs first) (up to approximately 36 months)

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	154			
Units: months				
median (confidence interval 95%)	6.3 (5.85 to 6.41)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS, defined as the time from initiation of study treatment to death from any cause.

End point type	Secondary

End point timeframe:

Baseline until death (up to approximately 36 months)

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: months				
median (confidence interval 95%)	10.0 (8.60 to 11.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

ORR, defined as the percentage of participants with a complete response (CR) or partial response (PR) on two consecutive occasions >= 4 weeks apart, as determined by the investigator according to Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1).

End point type	Secondary

End point timeframe:

Baseline up to approximately 36 months

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	154			
Units: Percentage of Participants				
number (not applicable)				
ORR during study: Yes	68.83			
ORR during study: No	31.17			

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 first occurrence of a documented objective response to disease progression or death from any cause (whichever occurs first), as determined by the investigator according to RECIST v1.1.

End point type	Secondary

End point timeframe:

Baseline to disease progression or death from any cause (whichever occurs first) up to approximately 36 months

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: months				
median (confidence interval 95%)	5.2 (4.86 to 5.59)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

DCR, defined as PR, CR and stable disease (SD) as determined by the investigator according to RECIST v1.1.

End point type	Secondary

End point timeframe:

Baseline up to approximately 36 months

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	147			
Units: percentage				
number (not applicable)				
DCR during study: Yes	93.20			
DCR during study: No	6.80			

Statistical analyses

No statistical analyses for this end point

Secondary: PFS Rate at 6 Months and 1 Year

End point title	PFS Rate at 6 Months and 1 Year

End point description:

PFS rate at 6 months and 1 year, defined as the proportion of patients who have not experienced disease progression or death from any cause at 6 months and 1 year separately, as determined by the investigator according to RECIST v1.1.

End point type	Secondary

End point timeframe:

Baseline up to 1 year

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	154			
Units: percentage				
number (confidence interval 95%)				
PFS at 6 months	55.84 (47.64 to 63.27)			
PFS at 12 months	13.36 (8.53 to 19.28)			

Statistical analyses

No statistical analyses for this end point

Secondary: OS Rate at 6 months, 12 months, 18 months and 24 months

End point title	OS Rate at 6 months, 12 months, 18 months and 24 months

End point description:

OS rate at 6 months, 12 months, 18 months and 24 months, defined as the proportion of patients who have not experienced death from any cause at 6 months, 12 months, 18 months and 24 months.

End point type	Secondary

End point timeframe:

Baseline to 24 months or death, whichever occurs first

End point values	Atezolizumab + Cisplatin/Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	154			
Units: percentage of participants				
number (confidence interval 95%)				
OS at 6 months	76.13 (68.60 to 82.09)			
OS at 12 months	41.73 (33.90 to 49.37)			
OS at 18 months	24.53 (18.02 to 31.59)			
OS at 24 months	17.72 (12.10 to 24.22)			

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 inclusion to treatment discontinuation for any reason.

End point type	Secondary

End point timeframe:

Baseline up to approximately 36 months

End point values	Atezolizumab + Cisplatin/Carbo platin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: months				
median (confidence interval 95%)	5.9 (5.12 to 6.45)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline up to 24 months

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	v25.1

Reporting groups

Reporting group title	Atezolizumab + Cisplatin/Carboplatin + Etoposide

Reporting group description:

Participants will receive the following treatment regimen: atezolizumab + cisplatin/carboplatin + etoposide. Induction treatment will be administered on a 21-day cycle for four or six cycles (according to investigator's choice). Following the induction phase, participants will continue maintenance therapy with atezolizumab. Participants will be treated until loss of clinical benefit, or unaccepted toxicity, or withdrawal of consent, or death (whichever occurs first).

Serious adverse events	Atezolizumab + Cisplatin/Carboplatin + Etoposide		
Total subjects affected by serious adverse events			
subjects affected / exposed	76 / 155 (49.03%)		
number of deaths (all causes)	128		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder Transitional Cell Carcinoma			
subjects affected / exposed	1 / 155 (0.65%)		
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	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Embolism			
subjects affected / exposed	1 / 155 (0.65%)		
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	2 / 155 (1.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	2 / 155 (1.29%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Pyrexia				
subjects affected / exposed	4 / 155 (2.58%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Respiratory Failure				
subjects affected / exposed	4 / 155 (2.58%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Acute Respiratory Failure				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pneumonitis				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Pneumothorax				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary Embolism				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory Acidosis				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional State				
subjects affected / exposed	2 / 155 (1.29%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Disorientation				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Neutrophil Count Decreased				
subjects affected / exposed	2 / 155 (1.29%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Platelet Count Decreased				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
White Blood Cell Count Decreased				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Injury, poisoning and procedural complications			
Radiation Oesophagitis			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Atrial Flutter			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac Failure			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-Respiratory Arrest			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Nervous System Disorder			
subjects affected / exposed	2 / 155 (1.29%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	2 / 155 (1.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ataxia			

subjects affected / exposed	2 / 155 (1.29%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Paraneoplastic Myelopathy				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular Accident				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cognitive Disorder				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune-Mediated Encephalitis				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Optic Neuritis				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Myoclonus				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral Infarction				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Paraparesis				

subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal Cord Compression				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 155 (0.65%)			
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	4 / 155 (2.58%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Thrombocytopenia				
subjects affected / exposed	1 / 155 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	2 / 155 (1.29%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	2 / 155 (1.29%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Febrile Neutropenia				
subjects affected / exposed	18 / 155 (11.61%)			
occurrences causally related to treatment / all	3 / 23			
deaths causally related to treatment / all	0 / 1			
Myelosuppression				

subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Visual Impairment			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	3 / 155 (1.94%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Enterocolitis			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal Disorder			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal Ischaemia			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Intestinal Obstruction			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Nausea			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Small Intestinal Perforation			

subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Chlolecystitis			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatotoxicity			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	4 / 155 (2.58%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Nephritis			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Immune-Mediated Myositis			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Back Pain			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	4 / 155 (2.58%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Fournier's Gangrene			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cellulitis			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 Pneumonia			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Anal Abscess			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			
subjects affected / exposed	2 / 155 (1.29%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	3 / 155 (1.94%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
COVID-19			

subjects affected / exposed	3 / 155 (1.94%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Pneumonia Staphylococcal			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic Shock			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory Tract Infection			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suspected COVID-19			
subjects affected / exposed	1 / 155 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	2 / 155 (1.29%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Hypoglycaemia			
subjects affected / exposed	1 / 155 (0.65%)		
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	Atezolizumab + Cisplatin/Carboplatin + Etoposide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	153 / 155 (98.71%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 155 (5.16%)		
occurrences (all)	8		
General disorders and administration site conditions			
Oedema Peripheral			
subjects affected / exposed	23 / 155 (14.84%)		
occurrences (all)	25		
Asthenia			
subjects affected / exposed	79 / 155 (50.97%)		
occurrences (all)	111		
Pain			
subjects affected / exposed	12 / 155 (7.74%)		
occurrences (all)	12		
Gait Disturbance			
subjects affected / exposed	13 / 155 (8.39%)		
occurrences (all)	14		
Mucosal Inflammation			
subjects affected / exposed	17 / 155 (10.97%)		
occurrences (all)	18		
Chest Pain			
subjects affected / exposed	18 / 155 (11.61%)		
occurrences (all)	20		
Fatigue			
subjects affected / exposed	22 / 155 (14.19%)		
occurrences (all)	26		
Pyrexia			
subjects affected / exposed	23 / 155 (14.84%)		
occurrences (all)	33		
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	34 / 155 (21.94%)		
occurrences (all)	39		
Dyspnoea			
subjects affected / exposed	34 / 155 (21.94%)		
occurrences (all)	37		
Productive Cough			
subjects affected / exposed	8 / 155 (5.16%)		
occurrences (all)	9		
Psychiatric disorders			
Depression			
subjects affected / exposed	8 / 155 (5.16%)		
occurrences (all)	8		
Anxiety			
subjects affected / exposed	10 / 155 (6.45%)		
occurrences (all)	10		
Insomnia			
subjects affected / exposed	13 / 155 (8.39%)		
occurrences (all)	13		
Investigations			
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	8 / 155 (5.16%)		
occurrences (all)	9		
Blood Creatinine Increased			
subjects affected / exposed	14 / 155 (9.03%)		
occurrences (all)	22		
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	15 / 155 (9.68%)		
occurrences (all)	20		
Aspartate Aminotransferase Increased			
subjects affected / exposed	17 / 155 (10.97%)		
occurrences (all)	34		
Alanine Aminotransferase Increased			
subjects affected / exposed	18 / 155 (11.61%)		
occurrences (all)	35		
Platelet Count Decreased			

subjects affected / exposed	20 / 155 (12.90%)		
occurrences (all)	39		
Neutrophil Count Decreased			
subjects affected / exposed	29 / 155 (18.71%)		
occurrences (all)	56		
White Blood Cell Count Decreased			
subjects affected / exposed	8 / 155 (5.16%)		
occurrences (all)	18		
Nervous system disorders			
Headache			
subjects affected / exposed	24 / 155 (15.48%)		
occurrences (all)	28		
Dizziness			
subjects affected / exposed	16 / 155 (10.32%)		
occurrences (all)	22		
Dysgeusia			
subjects affected / exposed	9 / 155 (5.81%)		
occurrences (all)	10		
Paraesthesia			
subjects affected / exposed	13 / 155 (8.39%)		
occurrences (all)	16		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	24 / 155 (15.48%)		
occurrences (all)	36		
Neutropenia			
subjects affected / exposed	51 / 155 (32.90%)		
occurrences (all)	77		
Anaemia			
subjects affected / exposed	72 / 155 (46.45%)		
occurrences (all)	97		
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	10 / 155 (6.45%)		
occurrences (all)	12		
Dysphagia			

subjects affected / exposed occurrences (all)	9 / 155 (5.81%) 9		
Dry Mouth subjects affected / exposed occurrences (all)	8 / 155 (5.16%) 8		
Abdominal Pain subjects affected / exposed occurrences (all)	12 / 155 (7.74%) 14		
Vomiting subjects affected / exposed occurrences (all)	27 / 155 (17.42%) 33		
Diarrhoea subjects affected / exposed occurrences (all)	32 / 155 (20.65%) 55		
Nausea subjects affected / exposed occurrences (all)	41 / 155 (26.45%) 53		
Constipation subjects affected / exposed occurrences (all)	47 / 155 (30.32%) 58		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	15 / 155 (9.68%) 15		
Rash subjects affected / exposed occurrences (all)	15 / 155 (9.68%) 15		
Alopecia subjects affected / exposed occurrences (all)	33 / 155 (21.29%) 34		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	8 / 155 (5.16%) 9		
Endocrine disorders			

Hypothyrodism			
subjects affected / exposed	15 / 155 (9.68%)		
occurrences (all)	21		
Hyperthyroidism			
subjects affected / exposed	15 / 155 (9.68%)		
occurrences (all)	16		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	20 / 155 (12.90%)		
occurrences (all)	24		
Myalgia			
subjects affected / exposed	10 / 155 (6.45%)		
occurrences (all)	10		
Back Pain			
subjects affected / exposed	20 / 155 (12.90%)		
occurrences (all)	21		
Pain in Extremity			
subjects affected / exposed	12 / 155 (7.74%)		
occurrences (all)	12		
Infections and infestations			
Respiratory Tract Infection			
subjects affected / exposed	9 / 155 (5.81%)		
occurrences (all)	10		
Urinary Tract Infection			
subjects affected / exposed	11 / 155 (7.10%)		
occurrences (all)	12		
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	44 / 155 (28.39%)		
occurrences (all)	49		
Hypomagnesaemia			
subjects affected / exposed	18 / 155 (11.61%)		
occurrences (all)	20		
Hyponatraemia			
subjects affected / exposed	13 / 155 (8.39%)		
occurrences (all)	14		

Hyperglycaemia subjects affected / exposed occurrences (all)	12 / 155 (7.74%) 12		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 July 2020	- The new Nanostring GeoMx® Digital Space Profiler (DSP) technology will be applied to the tissue samples submitted at baseline - The information about FoundationOneLiquid® was updated to reflect the current test specifications. - Exclusion Criteria section was clarified on patients who are positive for human immunodeficiency virus and who are allowed in the study. - 'Permitted Therapy' section added consolidation radiotherapy. - 'Tumor and Response Evaluation' section was clarified in case a PET-CT scan with no contrast was performed within permitted Screening window, it could be used as baseline test and was clarified that after completion of induction phase tumor assessment, tumor assessments will be required every 9 weeks thereafter. - In 'Laboratory Assessments and Biomarker Samples', for pregnancy test, added local practice is to do it in serum at every cycle. -In 'Screening and Baseline Assessments' section, information on validity of tumor assessments has been amended. - In 'Assessments during Treatment' section, information on validity of tests was amended. - Option to switch from cisplatin to carboplatin due to inacceptable toxicity was included in chemotherapy management sections. - Text of sections 'Subgroup Analyses', 'Biomarker Analyses' and Interim Analyses was updated to reflect statistical plan as per current Protocol. - CTCAE version was updated from v.4 to v.5. - The 30-day timeframe to report special situations and non serious AEs associated with special situations is specified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported