Clinical trial results:
A Phase I/III, Randomized, Double-Blind, Placebo-Controlled Study of Carboplatin Plus Etoposide With or Without Atezolizumab (Anti-PD-L1 Antibody) in Patients With Untreated Extensive-Stage Small Cell Lung Cancer

Summary

EudraCT number	2015-004861-97
Trial protocol	DE PL HU CZ GB AT GR ES FR IT
Global end of trial date	

Results information

Result version number	v1
This version publication date	05 May 2019
First version publication date	05 May 2019

Trial information

Trial identification

Sponsor protocol code	GO30081

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02763579
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@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	Interim
Date of interim/final analysis	24 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 April 2018
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This randomized, Phase I/III, multicenter, double-blinded, placebo-controlled study was designed to evaluate the safety and efficacy of atezolizumab (anti-programmed death-ligand 1 [PD-L1] antibody) in combination with carboplatin plus (+) etoposide compared with treatment with placebo + carboplatin + etoposide in subjects with chemotherapy-naive extensive-stage small cell lung cancer.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 June 2016
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	Australia: 11
Country: Number of subjects enrolled	China: 1
Country: Number of subjects enrolled	Japan: 42
Country: Number of subjects enrolled	Korea, Republic of: 17
Country: Number of subjects enrolled	Taiwan: 9
Country: Number of subjects enrolled	Austria: 20
Country: Number of subjects enrolled	Czech Republic: 17
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Spain: 25
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	United Kingdom: 10
Country: Number of subjects enrolled	Mexico: 4
Country: Number of subjects enrolled	United States: 86
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	Chile: 6
Country: Number of subjects enrolled	Greece: 11
Country: Number of subjects enrolled	Hungary: 19
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Poland: 45
Country: Number of subjects enrolled	Russian Federation: 30
Country: Number of subjects enrolled	Serbia: 15

Worldwide total number of subjects	403
EEA total number of subjects	178

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)	217
From 65 to 84 years	184
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects in this study included: extensive-stage small cell lung cancer (ES-SCLC) with no prior systemic treatment for ES-SCLC.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Atezolizumab + Carboplatin + Etoposide

Arm description:

Subjects received intravenous infusions of atezolizumab 1200 milligrams (mg) in combination with carboplatin to achieve an initial target area under the concentration-time curve (AUC) of 5 milligrams per milliliter per minute (mg/mL/min) followed by etoposide 100 milligrams per square meter (mg/m^2) on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m^2 was administered alone. Thereafter, subjects received maintenance (Cycle 5 onward) atezolizumab 1200 mg on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	MPDL3280A, Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab intravenous infusion was administered at a dose of 1200 mg on Day 1 of each 21-day cycle during the induction phase (Cycles 1-4) and maintenance phase (Cycle 5 onward).

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

Dosage and administration details:

Carboplatin intravenous infusion to achieve an initial target AUC of 5 mg/mL/min was administered 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 intravenous infusion was administered 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).

Arm title	Placebo + Carboplatin + Etoposide

Arm description:

Subjects received intravenous infusions of placebo in combination with carboplatin to achieve an initial target AUC of 5 mg/mL/min followed by etoposide 100 mg/m^2 on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m^2 was administered alone. Thereafter, subjects received maintenance (Cycle 5 onward) placebo on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

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

Dosage and administration details:

Placebo intravenous infusion was administered on Day 1 of each 21-day cycle during the induction phase (Cycles 1-4) and maintenance phase (Cycle 5 onward).

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

Dosage and administration details:

Carboplatin intravenous infusion to achieve an initial target AUC of 5 mg/mL/min was administered 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 intravenous infusion was administered 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).

Number of subjects in period 1	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide
Started	201	202
Completed	0	0
Not completed	201	202
Adverse event, serious fatal	101	132
Consent withdrawn by subject	18	9
Physician decision	2	-
On-going in study	77	60
Lost to follow-up	3	1

Baseline characteristics

Reporting groups

Reporting group title	Atezolizumab + Carboplatin + Etoposide

Reporting group description:

Subjects received intravenous infusions of atezolizumab 1200 milligrams (mg) in combination with carboplatin to achieve an initial target area under the concentration-time curve (AUC) of 5 milligrams per milliliter per minute (mg/mL/min) followed by etoposide 100 milligrams per square meter (mg/m^2) on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m^2 was administered alone. Thereafter, subjects received maintenance (Cycle 5 onward) atezolizumab 1200 mg on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

Reporting group title	Placebo + Carboplatin + Etoposide

Reporting group description:

Subjects received intravenous infusions of placebo in combination with carboplatin to achieve an initial target AUC of 5 mg/mL/min followed by etoposide 100 mg/m^2 on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m^2 was administered alone. Thereafter, subjects received maintenance (Cycle 5 onward) placebo on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

Reporting group values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide	Total
Number of subjects	201	202	403
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	111	106	217
From 65-84 years	89	95	184
85 years and over	1	1	2
Age continuous			
Units: years			
arithmetic mean	63.8	63.6	
standard deviation	± 8.8	± 9.0	-
Gender categorical			
As reported from Electronic Case Report Form (eCRF).			
Units: Subjects			
Female	72	70	142
Male	129	132	261

End points

End points reporting groups

Reporting group title	Atezolizumab + Carboplatin + Etoposide

Reporting group description:

Subjects received intravenous infusions of atezolizumab 1200 milligrams (mg) in combination with carboplatin to achieve an initial target area under the concentration-time curve (AUC) of 5 milligrams per milliliter per minute (mg/mL/min) followed by etoposide 100 milligrams per square meter (mg/m^2) on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m^2 was administered alone. Thereafter, subjects received maintenance (Cycle 5 onward) atezolizumab 1200 mg on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

Reporting group title	Placebo + Carboplatin + Etoposide

Reporting group description:

Subjects received intravenous infusions of placebo in combination with carboplatin to achieve an initial target AUC of 5 mg/mL/min followed by etoposide 100 mg/m^2 on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m^2 was administered alone. Thereafter, subjects received maintenance (Cycle 5 onward) placebo on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

Primary: Duration of Progression-Free Survival (PFS) as Assessed by the Investigator Using RECIST v1.1

End point title	Duration of Progression-Free Survival (PFS) as Assessed by the Investigator Using RECIST v1.1

End point description:

End point type	Primary

End point timeframe:

Baseline until PD or death, whichever occurs first (up to approximately 23 months)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	202		
Units: Months				
median (confidence interval 95%)	5.2 (4.4 to 5.6)	4.3 (4.2 to 4.5)		

Statistical analyses

Statistical analysis title	Statistical Analysis for PFS
Comparison groups	Atezolizumab + Carboplatin + Etoposide v Placebo + Carboplatin + Etoposide

Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	Logrank
Parameter estimate	Stratified Hazard Ratio
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	0.96

Primary: Duration of Overall Survival (OS)

End point title	Duration of Overall Survival (OS)

End point description:

End point type	Primary

End point timeframe:

Baseline until death from any cause (up to approximately 23 months)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	202		
Units: Months				
median (confidence interval 95%)	12.3 (10.8 to 15.9)	10.3 (9.3 to 11.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis for OS
Comparison groups	Atezolizumab + Carboplatin + Etoposide v Placebo + Carboplatin + Etoposide
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0069
Method	Logrank
Parameter estimate	Stratified Hazard Ratio
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	0.91

Secondary: Percentage of Participants With Objective Response (OR) as Assessed by the Investigator Using RECIST v1.1

End point title	Percentage of Participants With Objective Response (OR) as Assessed by the Investigator Using RECIST v1.1

End point description:

End point type	Secondary

End point timeframe:

Baseline until partial response (PR) or complete response (CR), whichever occurs first (up to approximately 46 months)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[1]	0[2]		
Units: Percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[1] - Data will be analyzed at the time of study completion.

[2] - Data will be analyzed at the time of study completion.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) as Assessed by the Investigator Using RECIST v1.1

End point title	Duration of Response (DOR) as Assessed by the Investigator Using RECIST v1.1

End point description:

End point type	Secondary

End point timeframe:

First occurrence of PR or CR until PD or death, whichever occurs first (up to approximately 46 months)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	0[4]		
Units: Months				
median (standard deviation)	()	()		

Notes:

[3] - Data will be analyzed at the time of study completion.

[4] - Data will be analyzed at the time of study completion.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Alive and Without PD, as Assessed by the Investigator Using RECIST v1.1, at 6 Months and 1 Year

End point title	Percentage of Participants Alive and Without PD, as Assessed by the Investigator Using RECIST v1.1, at 6 Months and 1 Year

End point description:

End point type	Secondary

End point timeframe:

6 months, 1 year (up to approximately 46 months)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: Percentage				
number (not applicable)				

Notes:

[5] - Data will be analyzed at the time of study completion.

[6] - Data will be analyzed at the time of study completion.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Alive at 1 Year and 2 Years

End point title	Percentage of Participants Alive at 1 Year and 2 Years

End point description:

End point type	Secondary

End point timeframe:

1 year, 2 years (up to approximately 46 months)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[7]	0[8]		
Units: Percentage				
number (not applicable)				

Notes:

[7] - Data will be analyzed at the time of study completion.

[8] - Data will be analyzed at the time of study completion.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Deterioration (TTD) per European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ) Core 30 (C30) Score

End point title	Time to Deterioration (TTD) per European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ) Core 30 (C30) Score

End point description:

End point type	Secondary

End point timeframe:

Baseline until deterioration per symptom subscale (up to approximately 46 months)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[9]	0[10]		
Units: Month				
median (confidence interval 95%)	(to)	(to)		

Notes:

[9] - Data will be analyzed at the time of study completion.

[10] - Data will be analyzed at the time of study completion.

Statistical analyses

No statistical analyses for this end point

Secondary: TTD per EORTC QLQ Lung Cancer Module (LC13) Score

End point title	TTD per EORTC QLQ Lung Cancer Module (LC13) Score

End point description:

End point type	Secondary

End point timeframe:

Baseline until deterioration per symptom subscale (up to approximately 46 months)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[11]	0[12]		
Units: Month				
median (confidence interval 95%)	(to)	(to)		

Notes:

[11] - Data will be analyzed at the time of study completion.

[12] - Data will be analyzed at the time of study completion.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Adverse Events

End point title	Percentage of Participants with Adverse Events

End point description:

End point type	Secondary

End point timeframe:

Baseline until up to 90 days after end of treatment (up to approximately 46 months)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[13]	0[14]		
Units: Percentage				
number (not applicable)				

Notes:

[13] - Data will be analyzed at the time of study completion.

[14] - Data will be analyzed at the time of study completion.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anti-Therapeutic Antibodies (ATAs)

End point title	Percentage of Participants With Anti-Therapeutic Antibodies (ATAs)

End point description:

End point type	Secondary

End point timeframe:

Predose (0 hours [H]) on Day (D) 1 of Cycles (C) 1, 2, 3, 4, 8, 16, and every 8 cycles (Q8C) thereafter (cycle = 21 days) until treatment discontinuation (up to 46 months) and 120 days after last dose (up to

approximately 46 months overall)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[15]	0[16]		
Units: Percentage				
number (not applicable)				

Notes:

[15] - Data will be analyzed at the time of study completion.

[16] - Data will be analyzed at the time of study completion.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) of Atezolizumab

End point title	Maximum Observed Serum Concentration (Cmax) of Atezolizumab

End point description:

Atezolizumab infusion duration is 60 minutes for the first infusion and 30 minutes for subsequent infusions.

End point type	Secondary

End point timeframe:

Predose (0 H) and postdose (0.5 H) on D1 of C1; predose (0 H) on D1 of C2, 3, 4, 8, 16, and Q8C thereafter (cycle = 21 days) until treatment discontinuation (up to 46 months) and 120 days after last dose (up to approximately 46 months overall)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[17]	0[18]		
Units: mcg/mL				
geometric mean (standard deviation)	()	()		

Notes:

[17] - Data will be analyzed at the time of study completion.

[18] - Data will be analyzed at the time of study completion.

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Serum Concentration (Cmin) of Atezolizumab

End point title	Minimum Observed Serum Concentration (Cmin) of Atezolizumab

End point description:

Atezolizumab infusion duration is 60 minutes for the first infusion and 30 minutes for subsequent

infusions.

End point type	Secondary

End point timeframe:

Predose (0 H) on D1 of C1, 2, 3, 4, 8, 16, and Q8C thereafter (cycle = 21 days) until treatment discontinuation (up to 46 months) and 120 days after last dose (up to approximately 46 months overall)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[19]	0[20]		
Units: mcg/mL				
geometric mean (standard deviation)	()	()		

Notes:

[19] - Data will be analyzed at the time of study completion.

[20] - Data will be analyzed at the time of study completion.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Carboplatin

End point title	Plasma Concentration of Carboplatin

End point description:

End point type	Secondary

End point timeframe:

Predose (0 H) and 5-10 minutes before end/1 H after end of carboplatin infusion (infusion duration = 1 H) on D1 of C1 and C3 (cycle = 21 days)(up to approximately 46 months)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[21]	0[22]		
Units: mcg/mL				
geometric mean (standard deviation)	()	()		

Notes:

[21] - Data will be analyzed at the time of study completion.

[22] - Data will be analyzed at the time of study completion.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Etoposide

End point title	Plasma Concentration of Etoposide

End point description:

End point type	Secondary

End point timeframe:

Predose (0 H) and 5-10 minutes before end/1 H and 4H after end of etoposide infusion (infusion duration = 1 H) on D1 of C1 and C3 (cycle = 21 days)(up to approximately 46 months)

End point values	Atezolizumab + Carboplatin + Etoposide	Placebo + Carboplatin + Etoposide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[23]	0[24]		
Units: mcg/mL				
geometric mean (standard deviation)	()	()		

Notes:

[23] - Data will be analyzed at the time of study completion.

[24] - Data will be analyzed at the time of study completion.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first study drug administration to the data cutoff date: 24 April 2018.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Placebo + Carboplatin + Etoposide

Reporting group description:

Subjects received intravenous infusions of placebo in combination with carboplatin to achieve an initial target AUC of 5 mg/mL/min followed by etoposide 100 mg/m^2 on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m^2 was administered alone. Thereafter, subjects received maintenance (Cycle 5 onward) placebo on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

Reporting group title	Atezolizumab + Carboplatin + Etoposide

Reporting group description:

Subjects received intravenous infusions of atezolizumab 1200 milligrams (mg) in combination with carboplatin to achieve an initial target area under the concentration-time curve (AUC) of 5 milligrams per milliliter per minute (mg/mL/min) followed by etoposide 100 milligrams per square meter (mg/m^2) on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m^2 was administered alone. Thereafter, subjects received maintenance (Cycle 5 onward) atezolizumab 1200 mg on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

Serious adverse events	Placebo + Carboplatin + Etoposide	Atezolizumab + Carboplatin + Etoposide	
Total subjects affected by serious adverse events			
subjects affected / exposed	68 / 196 (34.69%)	74 / 198 (37.37%)	
number of deaths (all causes)	130	103	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
METASTATIC NEOPLASM			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUMOUR PAIN			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vascular disorders			
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIPHERAL ARTERY OCCLUSION			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPERIOR VENA CAVA SYNDROME			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOPHLEBITIS			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 196 (0.51%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHEST PAIN			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEATH			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
FATIGUE			

subjects affected / exposed	0 / 196 (0.00%)	3 / 198 (1.52%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 196 (0.51%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
NON−CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
subjects affected / exposed	0 / 196 (0.00%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	2 / 196 (1.02%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
BRONCHIAL OBSTRUCTION			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	2 / 196 (1.02%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

DYSPNOEA			
subjects affected / exposed	2 / 196 (1.02%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMOPTYSIS			
subjects affected / exposed	1 / 196 (0.51%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
HYPERCAPNIA			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	1 / 196 (0.51%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS			
subjects affected / exposed	2 / 196 (1.02%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOTHORAX			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	2 / 196 (1.02%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY OEDEMA			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY FAILURE			

subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
ALCOHOL ABUSE			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEPRESSION			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 196 (0.51%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 196 (0.51%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
LIVER FUNCTION TEST INCREASED			

subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLATELET COUNT DECREASED			
subjects affected / exposed	2 / 196 (1.02%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSAMINASES INCREASED			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
FEMUR FRACTURE			
subjects affected / exposed	1 / 196 (0.51%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEAD INJURY			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFUSION RELATED REACTION			
subjects affected / exposed	2 / 196 (1.02%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RADIATION OESOPHAGITIS			

subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
THORACIC VERTEBRAL FRACTURE			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	2 / 196 (1.02%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIOVENTRICULAR BLOCK COMPLETE			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC TAMPONADE			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIOPULMONARY FAILURE			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
PERICARDIAL EFFUSION			
subjects affected / exposed	1 / 196 (0.51%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
SUPRAVENTRICULAR TACHYCARDIA			

subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GUILLAIN−BARRE SYNDROME			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SOMNOLENCE			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL CORD OEDEMA			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
subjects affected / exposed	0 / 196 (0.00%)	3 / 198 (1.52%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRIGEMINAL NEURALGIA			

subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 196 (1.02%)	3 / 198 (1.52%)	
occurrences causally related to treatment / all	2 / 2	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
DISSEMINATED INTRAVASCULAR COAGULATION			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE NEUTROPENIA			
subjects affected / exposed	9 / 196 (4.59%)	5 / 198 (2.53%)	
occurrences causally related to treatment / all	9 / 9	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOCYTOSIS			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOPENIA			
subjects affected / exposed	1 / 196 (0.51%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
subjects affected / exposed	8 / 196 (4.08%)	7 / 198 (3.54%)	
occurrences causally related to treatment / all	8 / 8	7 / 7	
deaths causally related to treatment / all	0 / 0	1 / 1	
PANCYTOPENIA			
subjects affected / exposed	4 / 196 (2.04%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOCYTOPENIA			

subjects affected / exposed	4 / 196 (2.04%)	5 / 198 (2.53%)	
occurrences causally related to treatment / all	4 / 4	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL ADHESIONS			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LIP OEDEMA			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILEUS			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL HAEMORRHAGE			

subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRITIS			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FAECES DISCOLOURED			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC ULCER PERFORATION			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIVERTICULAR PERFORATION			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	1 / 196 (0.51%)	3 / 198 (1.52%)	
occurrences causally related to treatment / all	0 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS			
subjects affected / exposed	0 / 196 (0.00%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS ACUTE			

subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCTITIS			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
AUTOIMMUNE COLITIS			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	3 / 196 (1.53%)	3 / 198 (1.52%)	
occurrences causally related to treatment / all	2 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLANGITIS			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
JAUNDICE			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
RASH			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SKIN TOXICITY			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 196 (0.00%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUBULOINTERSTITIAL NEPHRITIS			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
AUTOIMMUNE THYROIDITIS			
subjects affected / exposed	0 / 196 (0.00%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 196 (0.00%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CLOSTRIDIUM DIFFICILE COLITIS			

subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYTOMEGALOVIRUS INFECTION			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 196 (0.00%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG ABSCESS			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG INFECTION			
subjects affected / exposed	3 / 196 (1.53%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIC SEPSIS			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	7 / 196 (3.57%)	9 / 198 (4.55%)	
occurrences causally related to treatment / all	1 / 8	4 / 12	
deaths causally related to treatment / all	1 / 3	1 / 1	
PULMONARY SEPSIS			

subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
PYOPNEUMOTHORAX			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 196 (0.51%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	2 / 196 (1.02%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 196 (0.00%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERGLYCAEMIA			

subjects affected / exposed	0 / 196 (0.00%)	2 / 198 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOKALAEMIA			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOMAGNESAEMIA			
subjects affected / exposed	1 / 196 (0.51%)	0 / 198 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPONATRAEMIA			
subjects affected / exposed	4 / 196 (2.04%)	1 / 198 (0.51%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo + Carboplatin + Etoposide	Atezolizumab + Carboplatin + Etoposide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	186 / 196 (94.90%)	190 / 198 (95.96%)	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	6 / 196 (3.06%)	15 / 198 (7.58%)	
occurrences (all)	8	20	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	19 / 196 (9.69%)	23 / 198 (11.62%)	
occurrences (all)	25	27	
CHEST PAIN			
subjects affected / exposed	12 / 196 (6.12%)	16 / 198 (8.08%)	
occurrences (all)	12	19	
FATIGUE			

subjects affected / exposed	49 / 196 (25.00%)	51 / 198 (25.76%)	
occurrences (all)	61	65	
OEDEMA PERIPHERAL			
subjects affected / exposed	7 / 196 (3.57%)	13 / 198 (6.57%)	
occurrences (all)	8	14	
PYREXIA			
subjects affected / exposed	16 / 196 (8.16%)	18 / 198 (9.09%)	
occurrences (all)	18	29	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	25 / 196 (12.76%)	18 / 198 (9.09%)	
occurrences (all)	29	22	
DYSPNOEA			
subjects affected / exposed	16 / 196 (8.16%)	19 / 198 (9.60%)	
occurrences (all)	17	22	
HAEMOPTYSIS			
subjects affected / exposed	10 / 196 (5.10%)	14 / 198 (7.07%)	
occurrences (all)	10	20	
OROPHARYNGEAL PAIN			
subjects affected / exposed	5 / 196 (2.55%)	12 / 198 (6.06%)	
occurrences (all)	6	15	
PRODUCTIVE COUGH			
subjects affected / exposed	9 / 196 (4.59%)	10 / 198 (5.05%)	
occurrences (all)	14	10	
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	13 / 196 (6.63%)	15 / 198 (7.58%)	
occurrences (all)	13	18	
Investigations			
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	45 / 196 (22.96%)	37 / 198 (18.69%)	
occurrences (all)	80	74	
PLATELET COUNT DECREASED			
subjects affected / exposed	28 / 196 (14.29%)	25 / 198 (12.63%)	
occurrences (all)	39	36	
WEIGHT DECREASED			

subjects affected / exposed	10 / 196 (5.10%)	20 / 198 (10.10%)	
occurrences (all)	11	20	
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	24 / 196 (12.24%)	18 / 198 (9.09%)	
occurrences (all)	43	35	
Injury, poisoning and procedural complications			
INFUSION RELATED REACTION			
subjects affected / exposed	8 / 196 (4.08%)	10 / 198 (5.05%)	
occurrences (all)	9	13	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	11 / 196 (5.61%)	19 / 198 (9.60%)	
occurrences (all)	14	22	
HEADACHE			
subjects affected / exposed	23 / 196 (11.73%)	24 / 198 (12.12%)	
occurrences (all)	25	28	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	67 / 196 (34.18%)	84 / 198 (42.42%)	
occurrences (all)	83	95	
LEUKOPENIA			
subjects affected / exposed	19 / 196 (9.69%)	24 / 198 (12.12%)	
occurrences (all)	32	42	
NEUTROPENIA			
subjects affected / exposed	66 / 196 (33.67%)	71 / 198 (35.86%)	
occurrences (all)	105	122	
THROMBOCYTOPENIA			
subjects affected / exposed	29 / 196 (14.80%)	31 / 198 (15.66%)	
occurrences (all)	44	45	
Gastrointestinal disorders			
CONSTIPATION			
subjects affected / exposed	58 / 196 (29.59%)	51 / 198 (25.76%)	
occurrences (all)	69	61	
DIARRHOEA			
subjects affected / exposed	30 / 196 (15.31%)	32 / 198 (16.16%)	
occurrences (all)	46	42	

NAUSEA			
subjects affected / exposed	64 / 196 (32.65%)	74 / 198 (37.37%)	
occurrences (all)	89	99	
STOMATITIS			
subjects affected / exposed	9 / 196 (4.59%)	11 / 198 (5.56%)	
occurrences (all)	9	11	
VOMITING			
subjects affected / exposed	31 / 196 (15.82%)	38 / 198 (19.19%)	
occurrences (all)	45	47	
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	68 / 196 (34.69%)	73 / 198 (36.87%)	
occurrences (all)	71	75	
PRURITUS			
subjects affected / exposed	9 / 196 (4.59%)	12 / 198 (6.06%)	
occurrences (all)	10	12	
RASH			
subjects affected / exposed	11 / 196 (5.61%)	14 / 198 (7.07%)	
occurrences (all)	13	21	
RASH MACULO−PAPULAR			
subjects affected / exposed	2 / 196 (1.02%)	10 / 198 (5.05%)	
occurrences (all)	3	10	
Endocrine disorders			
HYPERTHYROIDISM			
subjects affected / exposed	5 / 196 (2.55%)	11 / 198 (5.56%)	
occurrences (all)	5	11	
HYPOTHYROIDISM			
subjects affected / exposed	1 / 196 (0.51%)	20 / 198 (10.10%)	
occurrences (all)	1	20	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	13 / 196 (6.63%)	18 / 198 (9.09%)	
occurrences (all)	16	20	
BACK PAIN			
subjects affected / exposed	19 / 196 (9.69%)	17 / 198 (8.59%)	
occurrences (all)	21	17	

MUSCULOSKELETAL PAIN			
subjects affected / exposed	11 / 196 (5.61%)	12 / 198 (6.06%)	
occurrences (all)	13	14	
PAIN IN EXTREMITY			
subjects affected / exposed	6 / 196 (3.06%)	13 / 198 (6.57%)	
occurrences (all)	7	13	
Infections and infestations			
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	16 / 196 (8.16%)	14 / 198 (7.07%)	
occurrences (all)	19	16	
URINARY TRACT INFECTION			
subjects affected / exposed	5 / 196 (2.55%)	12 / 198 (6.06%)	
occurrences (all)	5	16	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	36 / 196 (18.37%)	54 / 198 (27.27%)	
occurrences (all)	39	62	
HYPOKALAEMIA			
subjects affected / exposed	17 / 196 (8.67%)	8 / 198 (4.04%)	
occurrences (all)	18	8	
HYPOMAGNESAEMIA			
subjects affected / exposed	9 / 196 (4.59%)	12 / 198 (6.06%)	
occurrences (all)	9	17	
HYPONATRAEMIA			
subjects affected / exposed	12 / 196 (6.12%)	10 / 198 (5.05%)	
occurrences (all)	14	10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 August 2016	Protocol was amended to include change of phase from Phase III to Phase I/III. A secondary objective and corresponding outcome measure has been added to evaluate the efficacy of atezolizumab + carboplatin + etoposide compared with placebo + carboplatin + etoposide as measured by investigator-assessed time to response (TTR). TTR will be assessed in the intent-to-treat (ITT) population for patients who had an objective response as determined by the investigator according to RECIST v1.1. Clarifications were made around eligibility criteria and study conduct.
29 August 2017	Protocol was amended to include modifications to the statistical analysis plan and the timing for the efficacy analyses for progression-free survival (PFS) and overall survival (OS).
06 March 2019	Protocol was amended to include additional language to the end of study definition to clarify that if the Sponsor decides to terminate the study, subjects who are still receiving study treatment or are in survival follow-up may be enrolled into an extension study or non-interventional study. The timing of the interim and final analysis were modified to be aligned with the statistical analysis plan.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported