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	07 July 2022

Results information

Result version number	v3 (current)
This version publication date	06 July 2023
First version publication date	05 May 2019
Version creation reason	

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	Final
Date of interim/final analysis	07 July 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 July 2022
Was the trial ended prematurely?	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	Yes
Long term follow-up rationale	Safety, Efficacy, Ethical reason
Long term follow-up duration	32 Months
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: 100
Country: Number of subjects enrolled	Japan: 42
Country: Number of subjects enrolled	Korea, Republic of: 17
Country: Number of subjects enrolled	Taiwan: 10
Country: Number of subjects enrolled	Austria: 20
Country: Number of subjects enrolled	Czechia: 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	503
EEA total number of subjects	168

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)	286
From 65 to 84 years	215
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 114 centers in 21 countries: United States of America, Poland, Japan, Russia, Spain, Austria, Hungary, Czech Republic, South Korea, Italy, Serbia, Australia, Greece, United Kingdom, Germany, Taiwan, France, Chile, Brazil, Mexico, and China.

Pre-assignment

Screening details:

Total study population included 503 participants. Global population included 403 participants. An additional 100 participants enrolled during the China Extension. Total China population included 10 Chinese participants from Global population plus 100 participants from the China extension.

Period 1

Period 1 title	Overall Period (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?	No
Arm title	Placebo + Carboplatin + Etoposide - Global

Arm description:

Participants in the Global population 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, participants 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	Active comparator
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	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).

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).

Arm title	Atezolizumab + Carboplatin + Etoposide - Global

Arm description:

Participants in the Global population 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, participants 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, RO5541267, 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	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).

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).

Arm title	Placebo + Carboplatin + Etoposide - China

Arm description:

Participants in the China population 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, participants 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	Active comparator
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	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).

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).

Arm title	Atezolizumab + Carboplatin + Etoposide - China

Arm description:

Participants in the China population 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, participants 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, RO5541267, 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	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).

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).

Number of subjects in period 1	Placebo + Carboplatin + Etoposide - Global	Atezolizumab + Carboplatin + Etoposide - Global	Placebo + Carboplatin + Etoposide - China
Started	202	201	53
Completed	0	0	0
Not completed	202	201	53
Consent withdrawn by subject	12	18	3
Physician decision	-	2	-
Study Terminated By Sponsor	21	26	3
Death	167	151	46
Lost to follow-up	2	4	1

Number of subjects in period 1	Atezolizumab + Carboplatin + Etoposide - China
Started	57
Completed	0
Not completed	57
Consent withdrawn by subject	3
Physician decision	1
Study Terminated By Sponsor	4
Death	48
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Period

Reporting group description:

The total study population included 503 participants. The Global population included 403 participants. An additional 100 participants enrolled during the China Extension. The total China population included 10 Chinese participants from the Global population plus 100 participants from the China extension. 10 participants were part of the Global as well as China populations.

Reporting group values	Overall Period	Total	
Number of subjects	503	503	
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)	286	286	
From 65-84 years	215	215	
85 years and over	2	2	
Age Continuous Units: years			
arithmetic mean	63.0		
standard deviation	± 8.9	-	
Sex: Female, Male			
As reported from Electronic Case Report Form (eCRF).			
Units: Participants			
Female	164	164	
Male	339	339	

End points

End points reporting groups

Reporting group title	Placebo + Carboplatin + Etoposide - Global

Reporting group description:

Participants in the Global population 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, participants 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 - Global

Reporting group description:

Participants in the Global population 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, participants 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 - China

Reporting group description:

Participants in the China population 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, participants 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 - China

Reporting group description:

Participants in the China population 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, participants 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.

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

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

End point description:

Progression is defined using Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.0), as at least 20% increase in the sum of the longest diameter of target lesions compared to baseline, or unequivocal progression in non-target lesion(s), or the appearance of new lesion(s).

End point type	Primary

End point timeframe:

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

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for the endpoint.

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

Statistical analyses

Statistical analysis title	PFS Statistical Analysis
Comparison groups	Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global
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) in the Global Population

End point title	Duration of Overall Survival (OS) in the Global Population[2]

End point description:

OS is defined as the time from randomization to death from any cause.

End point type	Primary

End point timeframe:

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

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for the endpoint.

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

Statistical analyses

Statistical analysis title	OS Statistical Analysis
Comparison groups	Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global
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 Rate (ORR) as Assessed by the Investigator Using RECIST v1.1 in the Global Population

End point title	Percentage of Participants With Objective Response Rate (ORR) as Assessed by the Investigator Using RECIST v1.1 in the Global Population[3]

End point description:

Objective response (OR) is defined as complete response (CR) or partial response (PR) as determined by the investigator according to RECIST v1.1.

End point type	Secondary

End point timeframe:

Baseline until partial response (PR) or complete response (CR), whichever occurs first (up to approximately 23 months)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for the endpoint.

End point values	Placebo + Carboplatin + Etoposide - Global	Atezolizumab + Carboplatin + Etoposide - Global		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	201		
Units: Percentage of participants				
number (confidence interval 95%)	76.7 (70.29 to 82.38)	74.1 (67.50 to 80.03)		

Statistical analyses

Statistical analysis title	ORR Statistical Analysis
Comparison groups	Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.37

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

End point title	Duration of Response (DOR) as Assessed by the Investigator Using RECIST v1.1 in the Global Population[4]

End point description:

DOR is defined as the time interval from first occurrence of a documented objective response to the time of disease progression as determined by the investigator using RECIST v1.1 or death from any cause, whichever comes first.

End point type	Secondary

End point timeframe:

First occurrence of PR or CR until PD or death, whichever occurs first (up to approximately 23 months)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for the endpoint.

End point values	Placebo + Carboplatin + Etoposide - Global	Atezolizumab + Carboplatin + Etoposide - Global		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	155	149		
Units: Months				
median (confidence interval 95%)	3.1 (2.9 to 3.9)	4.1 (3.5 to 4.2)		

Statistical analyses

Statistical analysis title	DOR Statistical Analysis
Comparison groups	Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global
Number of subjects included in analysis	304
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0063
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.715
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.562
upper limit	0.911

Secondary: PFS Rate at 6 Months and at 1 year in Global Population

End point title	PFS Rate at 6 Months and at 1 year in Global Population[5]

End point description:

PFS rates at 6 months and at 1 year is defined as the proportion of participants who are alive without disease progression 6 months and 1 year after randomization, respectively.

End point type	Secondary

End point timeframe:

6 months, 1 year

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for the endpoint.

End point values	Placebo + Carboplatin + Etoposide - Global	Atezolizumab + Carboplatin + Etoposide - Global		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	201		
Units: Percentage of participants				
number (confidence interval 95%)				
6 Months	22.39 (16.56 to 28.22)	30.86 (24.26 to 37.45)		
1 Year	5.35 (2.14 to 8.56)	12.62 (7.85 to 17.40)		

Statistical analyses

Statistical analysis title	PFS Rate 1 Year Statistical Analysis

Statistical analysis description:

PFS Rate at 1 year

Comparison groups	Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global

Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0133
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	7.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.52
upper limit	13.02

Statistical analysis title	PFS Rate 6 Months Statistical Analysis
Statistical analysis description:	
PFS Rate at 6 months	
Comparison groups	Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0593
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	8.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.33
upper limit	17.27

Secondary: OS Rate at 1 Year and 2 Years in the Global Population

End point title	OS Rate at 1 Year and 2 Years in the Global Population[6]

End point description:

OS rates at 1 and 2 years is defined as the proportion of participants who are alive 1 year and 2 years after randomization, respectively. Note: 999999=not estimable.

End point type	Secondary

End point timeframe:

1 year, 2 years

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: No statistical analysis for the endpoint.

End point values	Placebo + Carboplatin + Etoposide - Global	Atezolizumab + Carboplatin + Etoposide - Global		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	201		
Units: Percentage of participants				
number (not applicable)				
1 Year	38.23	51.69		
2 Years	999999	999999		

Statistical analyses

Statistical analysis title	OS Rate 1 Year Statistical Analysis
Statistical analysis description: OS Rate at 1 year	
Comparison groups	Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0095
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	13.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.29
upper limit	23.64

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

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 in the Global Population[7]

End point description:

TTD according to the EORTC QLQ-C30 and EORTC QLQ-LC13 measures were evaluated in each of the following linearly transformed symptom scores: cough, dyspnea (single item), dyspnea (multi-item subscale), chest pain, or arm/shoulder pain. The linear transformation gives each individual symptom subscale a possible score of 0 to 100. For the symptom to be considered "deteriorated," a score increase of ≥10 points above baseline must be held for at least two consecutive assessments or an initial score increase of ≥10 points is followed by death within 3 weeks from the last assessment. A ≥ 10-point change in the symptoms subscale score is perceived by participants as clinically significant. Note: 999999=not estimable; 000000=not estimable.

End point type	Secondary

End point timeframe:

Baseline until deterioration per symptom subscale (up to approximately 23 months)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for the endpoint.

End point values	Placebo + Carboplatin + Etoposide - Global	Atezolizumab + Carboplatin + Etoposide - Global		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	202	201		
Units: Month				
median (confidence interval 95%)				
Cough	999999 (16.6 to 999999)	20.3 (000000 to 999999)		
Pain in Chest	999999 (10.9 to 999999)	999999 (999999 to 999999)		
Pain in Arm or Shoulder	999999 (8.8 to 999999)	999999 (9.2 to 999999)		
Dyspnea	5.6 (3.6 to 8.8)	999999 (5.5 to 999999)		

Statistical analyses

Statistical analysis title	TTD Statistical Analysis Cough
Statistical analysis description: Cough	
Comparison groups	Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.3604
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.221
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.795
upper limit	1.874

Notes:

[8] - Stratified analysis. Stratification factors: Sex (male vs female) and ECOG (0 vs 1).

Statistical analysis title	TTD Statistical Analysis Pain in Arm or Shoulder
Statistical analysis description: Pain in Arm or Shoulder	
Comparison groups	Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global

Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.6922
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.077
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.747
upper limit	1.552

Statistical analysis title	TTD Statistical Analysis Dyspnea
Statistical analysis description:	
Dyspnea	
Comparison groups	Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.065
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.748
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.549
upper limit	1.019

Statistical analysis title	TTD Statistical Analysis Pain in Chest
Statistical analysis description:	
Pain in Chest	
Comparison groups	Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global
Number of subjects included in analysis	403
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.7712
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.058

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.722
upper limit	1.553

Notes:

[9] - Stratified analysis. Stratification factors: Sex (male vs female) and ECOG (0 vs 1).

Secondary: Maximum Observed Serum Concentration (Cmax) of Atezolizumab in the Global Population

End point title	Maximum Observed Serum Concentration (Cmax) of Atezolizumab in the Global Population[10]

End point description:

Atezolizumab maximum observed plasma concentration (Cmax; 30 minutes following the end of the atezolizumab infusion) for each respective day.

End point type	Secondary

End point timeframe:

Post-dose Day 1 of Cycle 1 (cycle length = 21 days)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for the endpoint.

End point values	Atezolizumab + Carboplatin + Etoposide - Global			
Subject group type	Reporting group			
Number of subjects analysed	185			
Units: µg/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1	389 (± 135)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with at Least One Adverse Event in the Global Population

End point title	Percentage of Participants with at Least One Adverse Event in the Global Population[11]

End point description:

The percentage of participants with at least one adverse event in the global population.

End point type	Secondary

End point timeframe:

Baseline until up to 90 days after end of treatment (up to approximately 49 months)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for the endpoint.

End point values	Placebo + Carboplatin + Etoposide - Global	Atezolizumab + Carboplatin + Etoposide - Global		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	198		
Units: Percentage of participants				
number (not applicable)	96.4	100.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anti-Drug Antibodies (ADA) to Atezolizumab in the Global Population

End point title	Percentage of Participants With Anti-Drug Antibodies (ADA) to Atezolizumab in the Global Population[12]

End point description:

The baseline prevalence and post-baseline incidence of ADAs against atezolizumab.

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 23 months) and 120 days after last dose (up to approximately 23 months overall)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for the endpoint.

End point values	Atezolizumab + Carboplatin + Etoposide - Global			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: Percentage of participants				
number (not applicable)				
Baseline evaluable participants (n=196)	2.0			
Post-baseline evaluable participants (n=188)	18.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Carboplatin in the Global Population

End point title	Plasma Concentration of Carboplatin in the Global Population[13]

End point description:

Plasma concentration of carboplatin in the Global population. Note: 999999=not estimable, D=Day, C=Cycle.

End point type	Secondary

End point timeframe:

Predose, before end of infusion, and after end of carboplatin infusion on Day 1 of Cycle 1 and Cycle 3 (cycle = 21 days)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for the endpoint.

End point values	Placebo + Carboplatin + Etoposide - Global	Atezolizumab + Carboplatin + Etoposide - Global		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: ng/mL				
arithmetic mean (standard deviation)				
Pre-Dose on D1 of C1 (n=12, 11)	999999 (± 999999)	999999 (± 999999)		
Before End of Infusion on D1 of C1 (n=12, 11)	13300 (± 4880)	11200 (± 5060)		
Post Infusion on D1 of C1 (n=11, 12)	7200 (± 1880)	6860 (± 1670)		
Pre-Dose on D1 of C3 (n=12, 13)	144 (± 58.3)	126 (± 48.1)		
Before End of Infusion on D1 of C3 (n=13, 13)	13900 (± 3590)	11300 (± 5090)		
Post Infusion on D1 of C3 (n=13, 13)	7180 (± 1630)	6540 (± 2200)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Serum Concentration (Cmin) of Atezolizumab in the Global Population

End point title	Minimum Observed Serum Concentration (Cmin) of Atezolizumab in the Global Population[14]

End point description:

Atezolizumab pre-dose plasma concentration (Cmin) for each respective day. Note: 999999=not estimable.

End point type	Secondary

End point timeframe:

Predose on Day 1 of Cycles 1, 3, 4, 8, 16 and 24 (cycle length = 21 days)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for the endpoint.

End point values	Atezolizumab + Carboplatin + Etoposide - Global			
Subject group type	Reporting group			
Number of subjects analysed	194			
Units: µg/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (n=194)	999999 (± 999999)			
Cycle 3 Day 1 (n=174)	80.6 (± 32.1)			
Cycle 4 Day 1 (n=156)	138 (± 56.4)			
Cycle 8 Day 1 (n=88)	186 (± 73.5)			
Cycle 16 Day 1 (n=22)	196 (± 63.1)			
Cycle 24 Day 1 (n=4)	221 (± 43.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Etoposide in the Global Population

End point title	Plasma Concentration of Etoposide in the Global Population[15]

End point description:

Plasma concentration of etoposide in the Global Population. Note: 999999=not estimable, C=Cycle, D=Day.

End point type	Secondary

End point timeframe:

Predose, before end of infusion, 1 and 4 hours after end of carboplatin infusion on Day 1 of Cycle 1 and Cycle 3 (cycle = 21 days)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for the endpoint.

End point values	Placebo + Carboplatin + Etoposide - Global	Atezolizumab + Carboplatin + Etoposide - Global		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: ng/mL				
arithmetic mean (standard deviation)				
Pre-Dose on D1 of C1 (n=12, 13)	999999 (± 999999)	999999 (± 999999)		
Before End of Infusion on D1 of C1 (n=10, 10)	17000 (± 3640)	19400 (± 2860)		
1 Hour Post Infusion on D1 of C1 (n=8, 12)	11100 (± 2010)	12600 (± 1960)		
4 Hours Post Infusion on D1 of C1 (n=9, 9)	7640 (± 2360)	7300 (± 1230)		
Pre-Dose on D1 of C3 (n=13, 13)	999999 (± 999999)	999999 (± 999999)		

Before End of Infusion on D1 of C3 (n=11, 9)	16600 (± 2180)	17700 (± 3600)		
1 Hour Post Infusion on D1 of C3 (n=10, 13)	12400 (± 3740)	12200 (± 2810)		
4 Hours Post Infusion on D1 of C3 (n=10, 11)	6740 (± 1230)	7960 (± 2090)		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

From the first study drug administration to the data cutoff date: 7 July 2022 (up to 49 months).

Adverse event reporting additional description:

Adverse events reported based on safety population, which included participants who received any amount of any component of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Placebo + Carboplatin + Etoposide - Global

Reporting group description:

Participants in the Global population 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, participants 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 - China

Reporting group description:

Participants in the China population 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, participants 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 - China

Reporting group description:

Participants in the China population 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, participants 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 - Global

Reporting group description:

Participants in the Global population 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, participants 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 - Global	Atezolizumab + Carboplatin + Etoposide - China	Placebo + Carboplatin + Etoposide - China
Total subjects affected by serious adverse events			
subjects affected / exposed	69 / 196 (35.20%)	22 / 57 (38.60%)	14 / 52 (26.92%)
number of deaths (all causes)	164	48	46
number of deaths resulting from adverse events	3	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraneoplastic syndrome			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic neoplasm			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis limb			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery occlusion			

subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 196 (0.00%)	2 / 57 (3.51%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 2	0 / 0
Pain			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza like illness			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pulmonary oedema			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			

subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial obstruction			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 196 (1.02%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 196 (1.02%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	2 / 196 (1.02%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hypercapnia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	2 / 196 (1.02%)	0 / 57 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			

subjects affected / exposed	2 / 196 (1.02%)	2 / 57 (3.51%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Platelet count decreased			
subjects affected / exposed	2 / 196 (1.02%)	4 / 57 (7.02%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	2 / 2	4 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	1 / 196 (0.51%)	2 / 57 (3.51%)	2 / 52 (3.85%)
occurrences causally related to treatment / all	1 / 1	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood alkaline phosphatase increased			

subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	1 / 196 (0.51%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test increased			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			

subjects affected / exposed	2 / 196 (1.02%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation oesophagitis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb injury			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	3 / 196 (1.53%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			

subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palpitations			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trigeminal neuralgia			

subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysarthria			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord oedema			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Pancytopenia			

subjects affected / exposed	4 / 196 (2.04%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	2 / 196 (1.02%)	0 / 57 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	4 / 196 (2.04%)	0 / 57 (0.00%)	2 / 52 (3.85%)
occurrences causally related to treatment / all	4 / 4	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	8 / 196 (4.08%)	1 / 57 (1.75%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	8 / 8	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Granulocytopenia			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			

subjects affected / exposed	9 / 196 (4.59%)	1 / 57 (1.75%)	2 / 52 (3.85%)
occurrences causally related to treatment / all	9 / 9	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelosuppression			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer perforation			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal adhesions			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lip oedema			

subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faeces discoloured			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	3 / 196 (1.53%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune colitis			

subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	1 / 196 (0.51%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin toxicity			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			

subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Clostridium difficile colitis			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelitis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	10 / 196 (5.10%)	4 / 57 (7.02%)	4 / 52 (7.69%)
occurrences causally related to treatment / all	3 / 11	3 / 7	4 / 5
deaths causally related to treatment / all	1 / 3	0 / 0	0 / 0
Pyopneumothorax			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 196 (0.51%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Lung abscess			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 196 (1.02%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			

subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	4 / 196 (2.04%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			

subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Atezolizumab + Carboplatin + Etoposide - Global		
Total subjects affected by serious adverse events			
subjects affected / exposed	81 / 198 (40.91%)		
number of deaths (all causes)	155		
number of deaths resulting from adverse events	3		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Paraneoplastic syndrome			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Metastatic neoplasm			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour pain			

subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Peripheral arterial occlusive disease				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis limb				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral artery occlusion				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Superior vena cava syndrome				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest discomfort				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			

Pain				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Systemic inflammatory response syndrome				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Asthenia				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	3 / 198 (1.52%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Influenza like illness				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				

Pneumothorax				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchial obstruction				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				

subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercapnia				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Psychiatric disorders				
Alcohol abuse				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Platelet count decreased				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				

subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neutrophil count decreased				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
C-reactive protein increased				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood alkaline phosphatase increased				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood bilirubin increased				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
White blood cell count decreased				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver function test increased				

subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Alanine aminotransferase increased				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Head injury				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infusion related reaction				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Radiation oesophagitis				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thoracic vertebral fracture				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Limb injury				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				

Supraventricular tachycardia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiopulmonary failure			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac tamponade			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Palpitations			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			

subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebrovascular accident				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Somnolence				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Trigeminal neuralgia				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Guillain-Barre syndrome				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	3 / 198 (1.52%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuropathy peripheral				

subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dysarthria				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal cord oedema				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Pancytopenia				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	3 / 198 (1.52%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Leukocytosis				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	5 / 198 (2.53%)			
occurrences causally related to treatment / all	5 / 5			
deaths causally related to treatment / all	0 / 0			
Disseminated intravascular coagulation				

subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	7 / 198 (3.54%)			
occurrences causally related to treatment / all	7 / 7			
deaths causally related to treatment / all	1 / 1			
Granulocytopenia				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	5 / 198 (2.53%)			
occurrences causally related to treatment / all	4 / 5			
deaths causally related to treatment / all	0 / 0			
Myelosuppression				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Small intestinal obstruction				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer perforation				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal adhesions				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastritis				

subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lip oedema				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Faeces discoloured				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus				

subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	3 / 198 (1.52%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Proctitis				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Autoimmune colitis				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	3 / 198 (1.52%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticular perforation				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Drug-induced liver injury				

subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholangitis				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Jaundice				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Rash				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin toxicity				
subjects affected / exposed	1 / 198 (0.51%)			
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	2 / 198 (1.01%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Tubulointerstitial nephritis				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Autoimmune thyroiditis				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			

Inappropriate antidiuretic hormone secretion				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myalgia				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Clostridium difficile colitis				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myelitis				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	12 / 198 (6.06%)			
occurrences causally related to treatment / all	5 / 15			
deaths causally related to treatment / all	1 / 1			
Pyopneumothorax				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related sepsis				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung abscess				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenic sepsis				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus infection				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	2 / 198 (1.01%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				

subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Electrolyte imbalance			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypomagnesaemia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo + Carboplatin + Etoposide - Global	Atezolizumab + Carboplatin + Etoposide - China	Placebo + Carboplatin + Etoposide - China
Total subjects affected by non-serious adverse events			
subjects affected / exposed	187 / 196 (95.41%)	56 / 57 (98.25%)	52 / 52 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 196 (3.06%)	0 / 57 (0.00%)	2 / 52 (3.85%)
occurrences (all)	8	0	2

General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	5 / 196 (2.55%)	5 / 57 (8.77%)	2 / 52 (3.85%)
occurrences (all)	5	5	2
Asthenia			
subjects affected / exposed	20 / 196 (10.20%)	4 / 57 (7.02%)	4 / 52 (7.69%)
occurrences (all)	26	4	5
Chest pain			
subjects affected / exposed	14 / 196 (7.14%)	5 / 57 (8.77%)	4 / 52 (7.69%)
occurrences (all)	14	5	4
Oedema peripheral			
subjects affected / exposed	7 / 196 (3.57%)	1 / 57 (1.75%)	0 / 52 (0.00%)
occurrences (all)	8	1	0
Fatigue			
subjects affected / exposed	51 / 196 (26.02%)	6 / 57 (10.53%)	0 / 52 (0.00%)
occurrences (all)	67	8	0
Pyrexia			
subjects affected / exposed	16 / 196 (8.16%)	13 / 57 (22.81%)	4 / 52 (7.69%)
occurrences (all)	18	19	7
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	28 / 196 (14.29%)	14 / 57 (24.56%)	10 / 52 (19.23%)
occurrences (all)	33	20	12
Haemoptysis			
subjects affected / exposed	12 / 196 (6.12%)	4 / 57 (7.02%)	5 / 52 (9.62%)
occurrences (all)	12	4	6
Oropharyngeal pain			
subjects affected / exposed	5 / 196 (2.55%)	2 / 57 (3.51%)	0 / 52 (0.00%)
occurrences (all)	6	2	0
Productive cough			
subjects affected / exposed	9 / 196 (4.59%)	7 / 57 (12.28%)	5 / 52 (9.62%)
occurrences (all)	14	7	5
Dyspnoea			
subjects affected / exposed	17 / 196 (8.67%)	2 / 57 (3.51%)	2 / 52 (3.85%)
occurrences (all)	18	2	2
Psychiatric disorders			

Insomnia			
subjects affected / exposed	14 / 196 (7.14%)	4 / 57 (7.02%)	3 / 52 (5.77%)
occurrences (all)	14	8	9
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 196 (2.55%)	11 / 57 (19.30%)	9 / 52 (17.31%)
occurrences (all)	7	15	16
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 196 (1.53%)	1 / 57 (1.75%)	3 / 52 (5.77%)
occurrences (all)	3	2	4
Blood triglycerides increased			
subjects affected / exposed	0 / 196 (0.00%)	6 / 57 (10.53%)	4 / 52 (7.69%)
occurrences (all)	0	18	5
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 196 (0.51%)	2 / 57 (3.51%)	4 / 52 (7.69%)
occurrences (all)	1	2	4
Neutrophil count decreased			
subjects affected / exposed	45 / 196 (22.96%)	41 / 57 (71.93%)	33 / 52 (63.46%)
occurrences (all)	80	107	85
Blood creatinine increased			
subjects affected / exposed	3 / 196 (1.53%)	4 / 57 (7.02%)	3 / 52 (5.77%)
occurrences (all)	3	8	3
Protein urine present			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	3 / 52 (5.77%)
occurrences (all)	0	1	4
Blood glucose increased			
subjects affected / exposed	0 / 196 (0.00%)	3 / 57 (5.26%)	3 / 52 (5.77%)
occurrences (all)	0	3	3
Platelet count decreased			
subjects affected / exposed	30 / 196 (15.31%)	24 / 57 (42.11%)	14 / 52 (26.92%)
occurrences (all)	41	40	26
Blood cholesterol increased			
subjects affected / exposed	0 / 196 (0.00%)	8 / 57 (14.04%)	4 / 52 (7.69%)
occurrences (all)	0	23	4
Weight increased			

subjects affected / exposed	6 / 196 (3.06%)	1 / 57 (1.75%)	4 / 52 (7.69%)
occurrences (all)	7	1	4
Weight decreased			
subjects affected / exposed	10 / 196 (5.10%)	10 / 57 (17.54%)	6 / 52 (11.54%)
occurrences (all)	11	10	6
Blood bilirubin increased			
subjects affected / exposed	0 / 196 (0.00%)	2 / 57 (3.51%)	5 / 52 (9.62%)
occurrences (all)	0	2	6
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 196 (0.00%)	1 / 57 (1.75%)	3 / 52 (5.77%)
occurrences (all)	0	1	4
White blood cell count decreased			
subjects affected / exposed	24 / 196 (12.24%)	34 / 57 (59.65%)	29 / 52 (55.77%)
occurrences (all)	43	101	73
Haemoglobin decreased			
subjects affected / exposed	3 / 196 (1.53%)	4 / 57 (7.02%)	0 / 52 (0.00%)
occurrences (all)	3	6	0
Alanine aminotransferase increased			
subjects affected / exposed	6 / 196 (3.06%)	13 / 57 (22.81%)	10 / 52 (19.23%)
occurrences (all)	6	21	15
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	8 / 196 (4.08%)	1 / 57 (1.75%)	1 / 52 (1.92%)
occurrences (all)	9	1	1
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	1 / 196 (0.51%)	1 / 57 (1.75%)	4 / 52 (7.69%)
occurrences (all)	2	1	4
Nervous system disorders			
Dizziness			
subjects affected / exposed	11 / 196 (5.61%)	2 / 57 (3.51%)	2 / 52 (3.85%)
occurrences (all)	14	2	2
Headache			
subjects affected / exposed	23 / 196 (11.73%)	3 / 57 (5.26%)	3 / 52 (5.77%)
occurrences (all)	26	3	3
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	69 / 196 (35.20%)	46 / 57 (80.70%)	40 / 52 (76.92%)
occurrences (all)	84	76	50
Thrombocytopenia			
subjects affected / exposed	29 / 196 (14.80%)	17 / 57 (29.82%)	16 / 52 (30.77%)
occurrences (all)	44	27	31
Leukopenia			
subjects affected / exposed	19 / 196 (9.69%)	9 / 57 (15.79%)	14 / 52 (26.92%)
occurrences (all)	32	24	22
Neutropenia			
subjects affected / exposed	66 / 196 (33.67%)	11 / 57 (19.30%)	17 / 52 (32.69%)
occurrences (all)	105	32	41
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	58 / 196 (29.59%)	10 / 57 (17.54%)	8 / 52 (15.38%)
occurrences (all)	70	19	12
Abdominal distension			
subjects affected / exposed	2 / 196 (1.02%)	3 / 57 (5.26%)	1 / 52 (1.92%)
occurrences (all)	2	3	1
Stomatitis			
subjects affected / exposed	9 / 196 (4.59%)	1 / 57 (1.75%)	1 / 52 (1.92%)
occurrences (all)	9	1	1
Vomiting			
subjects affected / exposed	34 / 196 (17.35%)	14 / 57 (24.56%)	7 / 52 (13.46%)
occurrences (all)	49	20	7
Abdominal pain			
subjects affected / exposed	11 / 196 (5.61%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences (all)	11	0	0
Diarrhoea			
subjects affected / exposed	30 / 196 (15.31%)	4 / 57 (7.02%)	2 / 52 (3.85%)
occurrences (all)	46	5	2
Nausea			
subjects affected / exposed	65 / 196 (33.16%)	21 / 57 (36.84%)	10 / 52 (19.23%)
occurrences (all)	95	47	15
Hepatobiliary disorders			

Hepatic function abnormal			
subjects affected / exposed	0 / 196 (0.00%)	3 / 57 (5.26%)	3 / 52 (5.77%)
occurrences (all)	0	3	3
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	69 / 196 (35.20%)	25 / 57 (43.86%)	18 / 52 (34.62%)
occurrences (all)	72	26	18
Rash			
subjects affected / exposed	13 / 196 (6.63%)	6 / 57 (10.53%)	1 / 52 (1.92%)
occurrences (all)	15	9	1
Pruritus			
subjects affected / exposed	9 / 196 (4.59%)	2 / 57 (3.51%)	1 / 52 (1.92%)
occurrences (all)	10	3	1
Rash maculo-papular			
subjects affected / exposed	2 / 196 (1.02%)	0 / 57 (0.00%)	0 / 52 (0.00%)
occurrences (all)	3	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 196 (0.51%)	2 / 57 (3.51%)	7 / 52 (13.46%)
occurrences (all)	1	3	10
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 196 (0.51%)	8 / 57 (14.04%)	2 / 52 (3.85%)
occurrences (all)	1	9	2
Hyperthyroidism			
subjects affected / exposed	5 / 196 (2.55%)	2 / 57 (3.51%)	0 / 52 (0.00%)
occurrences (all)	5	2	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	18 / 196 (9.18%)	3 / 57 (5.26%)	0 / 52 (0.00%)
occurrences (all)	20	3	0
Pain in extremity			
subjects affected / exposed	8 / 196 (4.08%)	2 / 57 (3.51%)	2 / 52 (3.85%)
occurrences (all)	9	2	2
Arthralgia			

subjects affected / exposed	22 / 196 (11.22%)	1 / 57 (1.75%)	4 / 52 (7.69%)
occurrences (all)	29	1	4
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	6 / 196 (3.06%)	2 / 57 (3.51%)	5 / 52 (9.62%)
occurrences (all)	6	5	5
Upper respiratory tract infection			
subjects affected / exposed	17 / 196 (8.67%)	3 / 57 (5.26%)	2 / 52 (3.85%)
occurrences (all)	20	3	2
Nasopharyngitis			
subjects affected / exposed	2 / 196 (1.02%)	3 / 57 (5.26%)	4 / 52 (7.69%)
occurrences (all)	2	3	4
Metabolism and nutrition disorders			
Hypoproteinaemia			
subjects affected / exposed	0 / 196 (0.00%)	4 / 57 (7.02%)	3 / 52 (5.77%)
occurrences (all)	0	4	4
Hypoalbuminaemia			
subjects affected / exposed	2 / 196 (1.02%)	9 / 57 (15.79%)	5 / 52 (9.62%)
occurrences (all)	2	14	5
Hypochloraemia			
subjects affected / exposed	2 / 196 (1.02%)	5 / 57 (8.77%)	4 / 52 (7.69%)
occurrences (all)	3	6	7
Hypomagnesaemia			
subjects affected / exposed	10 / 196 (5.10%)	1 / 57 (1.75%)	2 / 52 (3.85%)
occurrences (all)	10	1	3
Hyponatraemia			
subjects affected / exposed	12 / 196 (6.12%)	10 / 57 (17.54%)	11 / 52 (21.15%)
occurrences (all)	14	12	17
Hyperglycaemia			
subjects affected / exposed	5 / 196 (2.55%)	4 / 57 (7.02%)	2 / 52 (3.85%)
occurrences (all)	7	4	3
Hypokalaemia			
subjects affected / exposed	17 / 196 (8.67%)	5 / 57 (8.77%)	5 / 52 (9.62%)
occurrences (all)	18	8	10
Hypertriglyceridaemia			

subjects affected / exposed	1 / 196 (0.51%)	3 / 57 (5.26%)	0 / 52 (0.00%)
occurrences (all)	1	3	0
Diabetes mellitus			
subjects affected / exposed	0 / 196 (0.00%)	0 / 57 (0.00%)	3 / 52 (5.77%)
occurrences (all)	0	0	3
Decreased appetite			
subjects affected / exposed	41 / 196 (20.92%)	13 / 57 (22.81%)	12 / 52 (23.08%)
occurrences (all)	45	22	16

Non-serious adverse events	Atezolizumab + Carboplatin + Etoposide - Global		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	191 / 198 (96.46%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	15 / 198 (7.58%)		
occurrences (all)	20		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences (all)	2		
Asthenia			
subjects affected / exposed	25 / 198 (12.63%)		
occurrences (all)	29		
Chest pain			
subjects affected / exposed	18 / 198 (9.09%)		
occurrences (all)	22		
Oedema peripheral			
subjects affected / exposed	13 / 198 (6.57%)		
occurrences (all)	14		
Fatigue			
subjects affected / exposed	52 / 198 (26.26%)		
occurrences (all)	66		
Pyrexia			
subjects affected / exposed	20 / 198 (10.10%)		
occurrences (all)	32		
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	22 / 198 (11.11%)		
occurrences (all)	28		
Haemoptysis			
subjects affected / exposed	14 / 198 (7.07%)		
occurrences (all)	20		
Oropharyngeal pain			
subjects affected / exposed	13 / 198 (6.57%)		
occurrences (all)	17		
Productive cough			
subjects affected / exposed	10 / 198 (5.05%)		
occurrences (all)	10		
Dyspnoea			
subjects affected / exposed	21 / 198 (10.61%)		
occurrences (all)	24		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	16 / 198 (8.08%)		
occurrences (all)	19		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	8 / 198 (4.04%)		
occurrences (all)	9		
Blood alkaline phosphatase increased			
subjects affected / exposed	8 / 198 (4.04%)		
occurrences (all)	8		
Blood triglycerides increased			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences (all)	4		
Neutrophil count decreased			
subjects affected / exposed	37 / 198 (18.69%)		
occurrences (all)	74		

Blood creatinine increased				
subjects affected / exposed	7 / 198 (3.54%)			
occurrences (all)	13			
Protein urine present				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences (all)	0			
Blood glucose increased				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences (all)	0			
Platelet count decreased				
subjects affected / exposed	26 / 198 (13.13%)			
occurrences (all)	38			
Blood cholesterol increased				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences (all)	0			
Weight increased				
subjects affected / exposed	3 / 198 (1.52%)			
occurrences (all)	3			
Weight decreased				
subjects affected / exposed	21 / 198 (10.61%)			
occurrences (all)	21			
Blood bilirubin increased				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences (all)	0			
Electrocardiogram QT prolonged				
subjects affected / exposed	0 / 198 (0.00%)			
occurrences (all)	0			
White blood cell count decreased				
subjects affected / exposed	18 / 198 (9.09%)			
occurrences (all)	35			
Haemoglobin decreased				
subjects affected / exposed	1 / 198 (0.51%)			
occurrences (all)	1			
Alanine aminotransferase increased				
subjects affected / exposed	6 / 198 (3.03%)			
occurrences (all)	13			

Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	10 / 198 (5.05%)		
occurrences (all)	13		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	2 / 198 (1.01%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness			
subjects affected / exposed	20 / 198 (10.10%)		
occurrences (all)	23		
Headache			
subjects affected / exposed	25 / 198 (12.63%)		
occurrences (all)	30		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	86 / 198 (43.43%)		
occurrences (all)	101		
Thrombocytopenia			
subjects affected / exposed	31 / 198 (15.66%)		
occurrences (all)	46		
Leukopenia			
subjects affected / exposed	24 / 198 (12.12%)		
occurrences (all)	44		
Neutropenia			
subjects affected / exposed	71 / 198 (35.86%)		
occurrences (all)	122		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	52 / 198 (26.26%)		
occurrences (all)	65		
Abdominal distension			
subjects affected / exposed	5 / 198 (2.53%)		
occurrences (all)	5		
Stomatitis			

subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	11 / 198 (5.56%) 11 40 / 198 (20.20%) 52 10 / 198 (5.05%) 10 34 / 198 (17.17%) 46 77 / 198 (38.89%) 112		
Hepatobiliary disorders Hepatic function abnormal subjects affected / exposed occurrences (all)	 0 / 198 (0.00%) 0		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash maculo-papular subjects affected / exposed occurrences (all)	 73 / 198 (36.87%) 75 15 / 198 (7.58%) 25 15 / 198 (7.58%) 17 11 / 198 (5.56%) 11		
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	 0 / 198 (0.00%) 0		
Endocrine disorders			

Hypothyroidism			
subjects affected / exposed	20 / 198 (10.10%)		
occurrences (all)	20		
Hyperthyroidism			
subjects affected / exposed	11 / 198 (5.56%)		
occurrences (all)	11		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	19 / 198 (9.60%)		
occurrences (all)	19		
Pain in extremity			
subjects affected / exposed	13 / 198 (6.57%)		
occurrences (all)	13		
Arthralgia			
subjects affected / exposed	25 / 198 (12.63%)		
occurrences (all)	31		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	13 / 198 (6.57%)		
occurrences (all)	18		
Upper respiratory tract infection			
subjects affected / exposed	15 / 198 (7.58%)		
occurrences (all)	19		
Nasopharyngitis			
subjects affected / exposed	4 / 198 (2.02%)		
occurrences (all)	5		
Metabolism and nutrition disorders			
Hypoproteinaemia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	3 / 198 (1.52%)		
occurrences (all)	5		
Hypochloraemia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences (all)	0		

Hypomagnesaemia			
subjects affected / exposed	13 / 198 (6.57%)		
occurrences (all)	19		
Hyponatraemia			
subjects affected / exposed	10 / 198 (5.05%)		
occurrences (all)	10		
Hyperglycaemia			
subjects affected / exposed	9 / 198 (4.55%)		
occurrences (all)	13		
Hypokalaemia			
subjects affected / exposed	9 / 198 (4.55%)		
occurrences (all)	9		
Hypertriglyceridaemia			
subjects affected / exposed	0 / 198 (0.00%)		
occurrences (all)	0		
Diabetes mellitus			
subjects affected / exposed	1 / 198 (0.51%)		
occurrences (all)	1		
Decreased appetite			
subjects affected / exposed	55 / 198 (27.78%)		
occurrences (all)	64		

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