Clinical trial results:
A Phase III, Open-Label, Randomized Study of Atezolizumab (MPDL3280A, Anti-PD-L1 Antibody) in Combination With Carboplatin+Paclitaxel With or Without Bevacizumab Compared With Carboplatin + Paclitaxel + Bevacizumab in Chemotherapy-Naïve Patients With Stage IV Non-Squamous Non-Small Cell Lung Cancer

Summary

EudraCT number	2014-003207-30
Trial protocol	LV AT DE BE ES BG NL LT PT FR SK IT
Global end of trial date	

Results information

Result version number	v1
This version publication date	20 September 2020
First version publication date	20 September 2020

Trial information

Trial identification

Sponsor protocol code	GO29436

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02366143
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland,
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, 42 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	13 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 September 2019
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the safety and efficacy of atezolizumab in combination with carboplatin+paclitaxel with or without bevacizumab compared with treatment with carboplatin+paclitaxel+bevacizumab in chemotherapy-naive patients with Stage IV non-squamous non-small cell lung cancer (NSCLC).

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	31 March 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 88
Country: Number of subjects enrolled	Argentina: 10
Country: Number of subjects enrolled	Austria: 12
Country: Number of subjects enrolled	Belgium: 16
Country: Number of subjects enrolled	Bulgaria: 10
Country: Number of subjects enrolled	Brazil: 27
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Switzerland: 14
Country: Number of subjects enrolled	Chile: 44
Country: Number of subjects enrolled	Germany: 94
Country: Number of subjects enrolled	Spain: 138
Country: Number of subjects enrolled	France: 72
Country: Number of subjects enrolled	Italy: 50
Country: Number of subjects enrolled	Japan: 93
Country: Number of subjects enrolled	Lithuania: 3
Country: Number of subjects enrolled	Latvia: 17
Country: Number of subjects enrolled	Mexico: 9
Country: Number of subjects enrolled	Netherlands: 39
Country: Number of subjects enrolled	Peru: 9
Country: Number of subjects enrolled	Portugal: 23
Country: Number of subjects enrolled	Russian Federation: 37
Country: Number of subjects enrolled	Singapore: 9

Country: Number of subjects enrolled	Slovakia: 8
Country: Number of subjects enrolled	Taiwan: 34
Country: Number of subjects enrolled	Ukraine: 74
Country: Number of subjects enrolled	United States: 266
Worldwide total number of subjects	1202
EEA total number of subjects	482

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)	664
From 65 to 84 years	531
85 years and over	7

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study included chemotherapy-naive subjects with metastatic non-squamous non-small cell lung cancer (NSCLC).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm B

Arm description:

Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin

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

Dosage and administration details:

Atezolizumab was administered as IV infusion at a dose of 1200 milligrams (mg) on Day 1 of each 21-day cycle until loss of clinical benefit.

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

Dosage and administration details:

Paclitaxel was administered as IV infusion at a dose of 200 milligrams per square meter (mg/m^2) on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first.

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

Dosage and administration details:

Carboplatin was administered at area under the concentration-time curve (AUC) 6 milligrams per milliliter per minute (mg/mL/min) on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first.

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

Dosage and administration details:

Bevacizumab was administered as IV infusion at a dose of 15 milligrams per kilogram (mg/kg) on Day 1 of each 21-day cycle until progressive disease, unacceptable toxicity, or death.

Arm title	Arm A

Arm description:

Atezolizumab+Paclitaxel+Carboplatin

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

Dosage and administration details:

Atezolizumab was administered as IV infusion at a dose of 1200 milligrams (mg) on Day 1 of each 21-day cycle until loss of clinical benefit.

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

Dosage and administration details:

Paclitaxel was administered as IV infusion at a dose of 200 milligrams per square meter (mg/m^2) on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first.

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

Dosage and administration details:

Carboplatin was administered at area under the concentration-time curve (AUC) 6 milligrams per milliliter per minute (mg/mL/min) on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first.

Arm title	Arm C

Arm description:

Bevacizumab+Paclitaxel+Carboplatin

Arm type	Active comparator
Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	Avastin
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Bevacizumab was administered as IV infusion at a dose of 15 milligrams per kilogram (mg/kg) on Day 1 of each 21-day cycle until progressive disease, unacceptable toxicity, or death.

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

Dosage and administration details:

Paclitaxel was administered as IV infusion at a dose of 200 milligrams per square meter (mg/m^2) on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first.

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

Dosage and administration details:

Carboplatin was administered at area under the concentration-time curve (AUC) 6 milligrams per milliliter per minute (mg/mL/min) on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first.

Number of subjects in period 1	Arm B	Arm A	Arm C
Started	400	402	400
Completed	0	0	0
Not completed	400	402	400
Adverse event, serious fatal	272	275	301
On-Going in Study	107	101	79
Ineligible	1	-	-
PI Move and Site Closure	-	1	1
Physician decision	2	1	1
Consent withdrawn by subject	15	21	16
Lost to follow-up	2	1	1
Randomization Error	-	-	1
Increased Microscopic RBCS on Urinalysis	1	-	-
Protocol deviation	-	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm B
Reporting group description: Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin	
Reporting group title	Arm A
Reporting group description: Atezolizumab+Paclitaxel+Carboplatin	
Reporting group title	Arm C
Reporting group description: Bevacizumab+Paclitaxel+Carboplatin	

Reporting group values	Arm B	Arm A	Arm C
Number of subjects	400	402	400
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	215	223	226
From 65-84 years	182	178	171
85 years and over	3	1	3
Age Continuous Units: Years			
arithmetic mean	63.0	62.3	63.1
standard deviation	± 9.5	± 9.2	± 9.3
Sex: Female, Male Units: Participants			
Female	160	161	161
Male	240	241	239
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	3	0	1
Asian	56	48	46
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	3	9	12
White	322	331	335
More than one race	3	4	0
Unknown or Not Reported	13	10	6

Reporting group values	Total		
Number of subjects	1202		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	664		
From 65-84 years	531		
85 years and over	7		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	482		
Male	720		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	4		
Asian	150		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	24		
White	988		
More than one race	7		
Unknown or Not Reported	29		

Subject analysis sets

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit

whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)

Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or

death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or

until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Reporting group values	Arm C (Bevacizumab+Paclitaxel+Carboplatin)	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects	336	359	337
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±	±	±

Sex: Female, Male Units: Participants			
Female			
Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
More than one race			
Unknown or Not Reported			

Reporting group values	Arm A (Atezolizumab+Paclitaxel+Carboplatin)	Arm C (Bevacizumab+Paclitaxel+Carboplatin)	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Number of subjects	350	338	400
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous Units: Years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female			
Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
More than one race			
Unknown or Not Reported			

Reporting group values	Arm C (Bevacizumab+Paclitaxel+Carboplatin)	Arm A (Atezolizumab+Paclitaxel+Carboplatin)	Arm B (Atezolizumab+Bevacizumab+Paclitaxel

			+ Carboplatin)
Number of subjects	400	348	190
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

Reporting group values	Arm C (Bevacizumab+Paclitaxel+Carboplatin)	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects	164	192	165
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			

Age Continuous Units: Years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

Reporting group values	Arm A (Atezolizumab+Paclitaxel+Carboplatin)	Arm A (Atezolizumab+Paclitaxel+Carboplatin)	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Number of subjects	185	402	224
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race			

Unknown or Not Reported			

Reporting group values	Arm C (Bevacizumab+Paclitaxel+Carboplatin)	Arm A (Atezolizumab+Paclitaxel+Carboplatin)	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Number of subjects	159	347	353
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

Reporting group values	Arm C (Bevacizumab+Paclitaxel+Carboplatin)	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects	331	235	196
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years)			

Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

Reporting group values	Arm A (Atezolizumab+Paclitaxel+Carboplatin)	Arm C (Bevacizumab+Paclitaxel+Carboplatin)	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Number of subjects	222	197	348
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian			

Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
More than one race			
Unknown or Not Reported			

Reporting group values	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)	Arm C (Bevacizumab+Paclitaxel+Carboplatin)	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Number of subjects	356	336	400
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	±	±	±
Sex: Female, Male			
Units: Participants			
Female			
Male			
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native			
Asian			
Native Hawaiian or Other Pacific Islander			
Black or African American			
White			
More than one race			
Unknown or Not Reported			

Reporting group values	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)	Arm C (Bevacizumab+Paclitaxel+Carboplatin)	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Number of subjects	393	394	389
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	 ±	 ±	 4.6 ±
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

Reporting group values	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Number of subjects	376	345	28
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	 2.9 ±	 ±	 ±
Sex: Female, Male Units: Participants			
Female Male			

Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

Reporting group values	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)	Arm C (Bevacizumab+Paclitaxel+Carboplatin)	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Number of subjects	35	24	325
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

Reporting group values	Arm C (Bevacizumab+Paclitaxel+Carboplatin)	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)	
Number of subjects	348	356	

Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years arithmetic mean standard deviation	±	±	
Sex: Female, Male Units: Participants			
Female Male			
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White More than one race Unknown or Not Reported			

End points reporting groups

Reporting group title	Arm B
Reporting group description: Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin	
Reporting group title	Arm A
Reporting group description: Atezolizumab+Paclitaxel+Carboplatin	
Reporting group title	Arm C
Reporting group description: Bevacizumab+Paclitaxel+Carboplatin	
Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol
Subject analysis set description: Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.	
Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol
Subject analysis set description: Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.	
Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol
Subject analysis set description: Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.	
Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol
Subject analysis set description: Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.	
Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol
Subject analysis set description: Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.	
Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol
Subject analysis set description: Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or	

until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or

death.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm A (Atezolizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Subject analysis set title	Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion

of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

Subject analysis set title	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

Primary: Progression Free Survival (PFS), as Determined by the Investigator in Arm B Versus Arm C in the Teff-high WT Population and ITT-WT Population

End point title	Progression Free Survival (PFS), as Determined by the Investigator in Arm B Versus Arm C in the Teff-high WT Population and ITT-WT Population

End point description:

Progression Free Survival (PFS), as Determined by the Investigator using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) in Arm B versus Arm C in the T-effector (Teff)-high wild type (WT) population and the intent-to-treat (ITT)-WT population.

End point type	Primary

End point timeframe:

Baseline until disease progression or death, whichever occurs first until data cut-off on 15 September 2017 (up to approximately 29 months)

End point values	Arm C (Bevacizumab +Paclitaxel+Carboplatin)	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	336	356		
Units: Months				
median (confidence interval 95%)				
Teff-high WT (Arm B n=155; Arm C=129)	6.8 (5.9 to 7.4)	11.3 (9.1 to 13.0)		
ITT-WT (Arm B n=356; Arm C=336)	6.8 (6.0 to 7.1)	8.3 (7.7 to 9.8)		

Statistical analyses

Statistical analysis title	PFS Statistical Analysis

Statistical analysis description:

ITT-WT population

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)

Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	0.74

Notes:

[1] - Stratified Analysis

Statistical analysis title	PFS Statistical Analysis

Statistical analysis description:

Teff-high WT Population

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	0.68

Primary: Overall Survival (OS) in Arm B Versus Arm C in ITT-WT Population

End point title	Overall Survival (OS) in Arm B Versus Arm C in ITT-WT Population

End point description:

End point type	Primary

End point timeframe:

Baseline until death until data cut-off on 22 January 2018 (up to approximately 34 months)

End point values	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	359	337		
Units: Months				
median (confidence interval 95%)	19.2 (17.0 to 23.8)	14.7 (13.3 to 16.9)		

Statistical analyses

Statistical analysis title	OS Statistical Analysis
Statistical analysis description: ITT-WT Population	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	696
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.0164
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.96

Notes:
[2] - Stratified Analysis

Primary: Overall Survival (OS) in Arm A Versus Arm C in ITT-WT Population

End point title	Overall Survival (OS) in Arm A Versus Arm C in ITT-WT Population
End point description: Overall Survival (OS) in Arm A Versus Arm C in ITT-WT Population	
End point type	Primary
End point timeframe: Baseline until death (up approximately 53 months)	

End point values	Arm A (Atezolizumab +Paclitaxel+Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	350	338		
Units: Months				
median (confidence interval 95%)	19.0 (15.7 to 21.5)	14.7 (12.9 to 17.1)		

Statistical analyses

Statistical analysis title	OS Statistical Analysis
Statistical analysis description: ITT-WT Population	
Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	688
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.0528
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.842
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.707
upper limit	1.002

Notes:

[3] - Stratified Analysis

Secondary: PFS, as Determined by the Independent Review Facility (IRF) in Arm B Versus Arm C in Teff-High-WT Population and ITT-WT Population

End point title	PFS, as Determined by the Independent Review Facility (IRF) in Arm B Versus Arm C in Teff-High-WT Population and ITT-WT Population
End point description: PFS, as determined by the independent review facility (IRF) Using RECIST v1.1 in Arm B versus Arm C in the T-effector (Teff)-high wild type (WT) population and the intent-to-treat (ITT)-WT population.	
End point type	Secondary
End point timeframe: Baseline until disease progression or death, whichever occurs first (up to approximately 29 months)	

End point values	Arm C (Bevacizumab +Paclitaxel+Carboplatin)	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	336	356		
Units: Months				
median (confidence interval 95%)				
Teff-high WT Population (Arm B n=155; Arm C n=129)	7.0 (6.1 to 8.1)	10.7 (8.4 to 13.0)		
ITT-WT Population (Arm B n=356; Arm C n=336)	7.0 (6.3 to 8.0)	8.5 (7.7 to 9.7)		

Statistical analyses

Statistical analysis title	PFS Statistical Analysis
Statistical analysis description: ITT-WT population	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.0002
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.85

Notes:
[4] - Stratified Analysis

Statistical analysis title	PFS Statistical Analysis
Statistical analysis description: Teff-high WT Population	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.564

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.418
upper limit	0.76

Notes:

[5] - Stratified Analysis

Secondary: PFS, as Determined by the Investigator in Arm B Versus Arm C in Teff High Population and ITT Population

End point title	PFS, as Determined by the Investigator in Arm B Versus Arm C in Teff High Population and ITT Population

End point description:

PFS, as determined by the investigator according to RECIST v1.1, in Arm B versus C in the Teff high population and ITT population.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death, whichever occurs first (up to approximately 29 months)

End point values	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400	400		
Units: Months				
median (confidence interval 95%)				
Teff-high (Arm B n=166; Arm C=148)	11.3 (9.1 to 13.0)	6.8 (5.8 to 7.3)		
ITT Population (Arm B n=400; Arm C=4008)	8.3 (7.9 to 9.8)	6.8 (6.0 to 7.1)		

Statistical analyses

Statistical analysis title	PFS Statistical Analysis

Statistical analysis description:

ITT Population

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	800
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.61

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.517
upper limit	0.72

Notes:

[6] - Stratified Analysis

Statistical analysis title	PFS Statistical Analysis

Statistical analysis description:

Teff-high Population

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	800
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.492
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.374
upper limit	0.649

Notes:

[7] - Stratified Analysis

Secondary: PFS, as Determined by the Investigator in Arm A Versus Arm B in Teff High-WT Population and ITT-WT Population

End point title	PFS, as Determined by the Investigator in Arm A Versus Arm B in Teff High-WT Population and ITT-WT Population

End point description:

PFS, as determined by the investigator according to RECIST v1.1, in Arm A versus B in the Teff high-WT population and ITT-WT population.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death, whichever occurs first (up to approximately 29 months)

End point values	Arm A (Atezolizumab +Paclitaxel+Carboplatin)	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	348	356		
Units: Months				
median (confidence interval 95%)				
Teff-high WT (Arm A n=161; Arm B n=155)	6.3 (5.6 to 7.8)	11.3 (9.1 to 13.0)		

ITT-WT (Arm A n=348; Arm C n=356)	6.3 (5.6 to 7.0)	8.3 (7.7 to 9.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS, as Determined by the Investigator in Arm B Versus Arm C by PD-L1 Subgroup

End point title	PFS, as Determined by the Investigator in Arm B Versus Arm C by PD-L1 Subgroup

End point description:

PFS as Determined by the Investigator according to RECIST v1.1, in Arm B Versus Arm C by PD-L1 Subgroup: TC2/3 or 1C2/3 and TC1/2/3 or IC1/2/3 (ITT-WT Population)

End point type	Secondary

End point timeframe:

Baseline until disease progression or death, whichever occurs first (up to approximately 29 months)

End point values	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	190	164		
Units: Months				
median (confidence interval 95%)				
TC2/3 or IC2/3 (Arm B n=129; Arm C n=115)	11.1 (8.3 to 13.0)	6.8 (5.8 to 7.7)		
TC1/2/3 or IC1/2/3 (Arm B n=190; Arm C n=164)	11.0 (8.3 to 12.5)	6.8 (5.8 to 7.3)		

Statistical analyses

Statistical analysis title	PFS Statistical Analysis

Statistical analysis description:

TC1/2/3 or IC1/2/3 Subgroup

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	354
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.486

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.386
upper limit	0.639

Notes:

[8] - Stratified Analysis

Statistical analysis title	PFS Statistical Analysis

Statistical analysis description:

TC2/3 or IC2/3 Subgroup

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	354
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.471
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.352
upper limit	0.647

Notes:

[9] - Stratified Analysis

Secondary: OS in Arm B Versus Arm C by PD-L1 Subgroup

End point title	OS in Arm B Versus Arm C by PD-L1 Subgroup

End point description:

OS in Arm B Versus Arm C by PD-L1 Subgroup: TC2/3 or 1C2/3 and TC1/2/3 or IC1/2/3 (ITT-WT Population)

End point type	Secondary

End point timeframe:

Baseline until death (up to approximately 34 months)

End point values	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	192	165		
Units: Months				
median (confidence interval 95%)				
TC 2/3 or IC2/3 (Arm B n=129; Arm C n=116)	22.2 (17.0 to 26.1)	16.7 (10.5 to 24.2)		
TC1/2/3 or IC1/2/3 (Arm B n=192; Arm C n=165)	22.5 (18.2 to 26.1)	16.4 (11.2 to 22.9)		

Statistical analyses

Statistical analysis title	OS Analysis by PD-L1 Subgroup
Statistical analysis description: TC2/3 or IC2/3, WT ITT	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	357
Analysis specification	Pre-specified
Analysis type	superiority[10]
P-value	= 0.2765
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.824
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.169

Notes:

[10] - Unstratified Analysis

Statistical analysis title	OS Analysis by PD-L1 Subgroup
Statistical analysis description: TC1/2/3 or IC1/2/3, WT ITT	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	357
Analysis specification	Pre-specified
Analysis type	superiority[11]
P-value	= 0.0829
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.771
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.575
upper limit	1.035

Notes:

[11] - Unstratified Analysis

Secondary: OS in Arm A Versus Arm C by PD-L1 Subgroup

End point title	OS in Arm A Versus Arm C by PD-L1 Subgroup

End point description:

OS in Arm A Versus Arm C by PD-L1 Subgroup: TC2/3 or 1C2/3 and TC1/2/3 or IC1/2/3 (ITT-WT Population)

End point type	Secondary

End point timeframe:

Baseline until death (up approximately 53 months)

End point values	Arm C (Bevacizumab +Paclitaxel+Carboplatin)	Arm A (Atezolizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	165	185		
Units: Months				
median (confidence interval 95%)				
TC2/3 or IC2/3 (Arm A n=124; Arm C n=116)	17.0 (10.3 to 22.9)	26.1 (20.5 to 40.0)		
TC1/2/3 or IC1/2/3 (Arm A n=185; Arm C n=165)	16.0 (11.2 to 20.1)	24.4 (20.2 to 28.1)		

Statistical analyses

Statistical analysis title	OS by PD-L1 Subgroup

Statistical analysis description:

TC2/3 or IC2/3 Population

Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	350
Analysis specification	Pre-specified
Analysis type	superiority[12]
P-value	= 0.0097
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.662
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.484
upper limit	0.907

Notes:

[12] - Unstratified Analysis

Statistical analysis title	OS by PD-L1 Subgroup

Statistical analysis description:

TC1/2/3 or IC1/2/3 ITT-WT

Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)

Number of subjects included in analysis	350
Analysis specification	Pre-specified
Analysis type	superiority[13]
P-value	= 0.0073
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.709
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.551
upper limit	0.913

Notes:

[13] - Unstratified Analysis

Secondary: OS in Arm B Versus Arm C in Teff High-WT Population, Teff High Population, and ITT Population

End point title	OS in Arm B Versus Arm C in Teff High-WT Population, Teff High Population, and ITT Population

End point description:

Note: 999999=Not estimable

End point type	Secondary

End point timeframe:

Baseline until death (up to approximately 34 months)

End point values	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400	400		
Units: Months				
median (confidence interval 95%)				
Teff High-WT (Arm B n=156; Arm C n=129)	25.0 (17.8 to 999999)	16.7 (12.4 to 999999)		
Teff High Population (Arm B n=166; Arm C n=148)	25.2 (19.1 to 999999)	16.7 (12.4 to 999999)		
ITT Population (Arm B n=400; Arm C n=400)	19.8 (17.4 to 24.2)	14.9 (13.4 to 17.1)		

Statistical analyses

Statistical analysis title	OS Statistical Analysis

Statistical analysis description:

Teff high-WT

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)

Number of subjects included in analysis	800
Analysis specification	Pre-specified
Analysis type	superiority[14]
P-value	= 0.2843
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.831
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.592
upper limit	1.167

Notes:

[14] - Stratified Analysis

Statistical analysis title	OS Statistical Analysis
Statistical analysis description:	
Teff high	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	800
Analysis specification	Pre-specified
Analysis type	superiority[15]
P-value	= 0.1861
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.802
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.579
upper limit	1.113

Notes:

[15] - Stratified Analysis

Statistical analysis title	OS Statistical Analysis
Statistical analysis description:	
ITT	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	800
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.006
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.764

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	0.926

Secondary: OS in Arm A Versus Arm C in Teff High-WT Population, Teff High Population, and ITT Population

End point title	OS in Arm A Versus Arm C in Teff High-WT Population, Teff High Population, and ITT Population

End point description:

End point type	Secondary

End point timeframe:

Baseline until death (up approximately 53 months)

End point values	Arm C (Bevacizumab +Paclitaxel+Carboplatin)	Arm A (Atezolizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400	402		
Units: Months				
median (confidence interval 95%)				
Teff-high WT (Arm A n=163; Arm C n=130)	16.3 (11.2 to 22.3)	21.3 (17.6 to 26.3)		
Teff-high Population (Arm A n=177; Arm C n=148)	16.7 (11.4 to 21.6)	21.0 (17.1 to 26.0)		
ITT Population (Arm A n=402; Arm C n=400)	15.0 (13.4 to 17.1)	19.0 (16.3 to 21.5)		

Statistical analyses

Statistical analysis title	OS Statistical Analysis

Statistical analysis description:

Teff high-WT

Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	802
Analysis specification	Pre-specified
Analysis type	superiority[16]
P-value	= 0.0894
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.786

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.595
upper limit	1.038

Notes:

[16] - Stratified Analysis

Statistical analysis title	OS Statistical Analysis

Statistical analysis description:

Teff high

Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	802
Analysis specification	Pre-specified
Analysis type	superiority[17]
P-value	= 0.1276
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.815
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.626
upper limit	1.061

Notes:

[17] - Stratified Analysis

Statistical analysis title	OS Statistical Analysis

Statistical analysis description:

ITT

Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	802
Analysis specification	Pre-specified
Analysis type	superiority[18]
P-value	= 0.0681
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.861
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.733
upper limit	1.011

Notes:

[18] - Stratified Analysis

Secondary: OS in Arm A Versus Arm B in Teff High-WT Population and ITT-WT Population

End point title	OS in Arm A Versus Arm B in Teff High-WT Population and ITT-

	WT Population

End point description:

End point type	Secondary

End point timeframe:

Baseline until death (up approximately 53 months)

End point values	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm A (Atezolizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	359	350		
Units: Months				
median (confidence interval 95%)				
Teff High-WT (Arm A n=163; Arm B n=156)	25.8 (19.1 to 32.6)	21.3 (17.6 to 26.3)		
ITT-WT (Arm A n=350; Arm B n=359)	19.5 (17.0 to 22.2)	19.0 (15.7 to 21.5)		

Statistical analyses

Statistical analysis title	OS Statistical Analysis

Statistical analysis description:

Teff high-WT ITT

Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin)
Number of subjects included in analysis	709
Analysis specification	Pre-specified
Analysis type	superiority[19]
P-value	= 0.4599
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.901
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.683
upper limit	1.188

Notes:

[19] - Stratified Analysis

Secondary: Duration of Response (DOR), as Determined By Investigator in Arm B Versus Arm C

End point title	Duration of Response (DOR), as Determined By Investigator in Arm B Versus Arm C

End point description:

DOR, as determined by investigator according to RECIST v1.1 in Arm B versus Arm C in the Teff high-WT population and the ITT-WT population.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death, whichever occurs first (up to approximately 29 months)

End point values	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	224	159		
Units: Months				
median (confidence interval 95%)				
Teff high-WT (Arm B n=106; Arm C n=68)	11.2 (9.7 to 15.7)	5.7 (4.9 to 7.0)		
ITT-WT (Arm B n=224; Arm C n=159)	9.0 (6.9 to 11.4)	5.7 (5.1 to 6.5)		

Statistical analyses

Statistical analysis title	DOR Statistical Analysis

Statistical analysis description:

ITT-WT

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	superiority[20]
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.523
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.406
upper limit	0.675

Notes:

[20] - Stratified Analysis

Statistical analysis title	DOR Statistical Analysis

Statistical analysis description:

Teff-high WT

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)

Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	superiority[21]
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.283
upper limit	0.624

Notes:

[21] - Stratified Analysis

Secondary: Percentage of Participants With an Objective Response (OR) (Complete Response [CR] or Partial Response [PR]) as Determined by the Investigator in the Teff-High-WT Population and ITT-WT Population

End point title	Percentage of Participants With an Objective Response (OR) (Complete Response [CR] or Partial Response [PR]) as Determined by the Investigator in the Teff-High-WT Population and ITT-WT Population

End point description:

Percentage of Participants With an Objective Response (OR) (Complete Response [CR] or Partial Response [PR]) as Determined by the Investigator using RECIST v1.1 in the Teff-High-WT population and ITT-WT population.

End point type	Secondary

End point timeframe:

Baseline until disease progression or death, whichever occurs first (up to approximately 29 months)

End point values	Arm A (Atezolizumab +Paclitaxel+Carboplatin)	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	347	353	331	
Units: Percentage				
number (not applicable)				
Teff-high WT (Arm A n=161; Arm B n=153)	54.0	69.3	53.5	
ITT-WT (Arm A n=347; Arm B n=353)	49.3	63.5	48.0	

Statistical analyses

No statistical analyses for this end point

Secondary: OS Rates at Years 1 and 2 in Arm B Versus Arm C

End point title	OS Rates at Years 1 and 2 in Arm B Versus Arm C

End point description:

OS at 1- and 2-year landmark timepoints in Teff-high WT population and ITT-WT population.

End point type	Secondary

End point timeframe:

Years 1 and 2 (up to approximately 34 months)

End point values	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	235	196		
Units: Percentage				
number (confidence interval 95%)				
1-Year Teff-high WT (Arm B n=105; Arm C n=71)	68.63 (61.28 to 75.98)	58.74 (50.03 to 67.45)		
1-Year ITT-WT (Arm B n=235; Arm C n=196)	67.32 (62.41 to 72.22)	60.63 (55.34 to 65.93)		
2-Year Teff-high WT (Arm B n=21; Arm C n=15)	52.03 (43.12 to 60.94)	41.70 (31.55 to 51.85)		
2-Year ITT-WT (Arm B n=34; Arm C n=29)	43.42 (36.94 to 49.90)	33.71 (27.44 to 39.98)		

Statistical analyses

Statistical analysis title	OS Rate at Year 1 Statistical Analysis

Statistical analysis description:

1-Year ITT-WT Population

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	431
Analysis specification	Pre-specified
Analysis type	superiority[22]
P-value	= 0.0697
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	6.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.54
upper limit	13.9

Notes:

[22] - Stratified Analysis

Statistical analysis title	OS Rate at Year 2 Statistical Analysis

Statistical analysis description:

2-Year ITT-WT Population

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	431
Analysis specification	Pre-specified
Analysis type	superiority[23]
P-value	= 0.0347
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	9.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	18.73

Notes:

[23] - Stratified Analysis

Statistical analysis title	OS Rate at Year 1 Statistical Analysis
Statistical analysis description: 1-Year Teff-high WT Population	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	431
Analysis specification	Pre-specified
Analysis type	superiority[24]
P-value	= 0.089
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	9.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.51
upper limit	21.29

Notes:

[24] - Stratified Analysis

Statistical analysis title	OS Rate at Year 2 Statistical Analysis
Statistical analysis description: 2-Year Teff-high WT Population	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	431
Analysis specification	Pre-specified
Analysis type	superiority[25]
P-value	= 0.1336
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	10.34

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.17
upper limit	23.84

Notes:

[25] - Stratified Analysis

Secondary: OS Rates at Years 1 and 2 in Arm A Versus Arm C

End point title	OS Rates at Years 1 and 2 in Arm A Versus Arm C

End point description:

OS at 1- and 2-year landmark timepoints in Teff-high WT population and ITT-WT population.

End point type	Secondary

End point timeframe:

Years 1 and 2 (up to approximately 53 months)

End point values	Arm A (Atezolizumab +Paclitaxel+Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	222	197		
Units: Percentage				
number (confidence interval 95%)				
1-Year Teff-high WT (Arm A n=110; Arm C n=72)	67.48 (60.29 to 74.68)	56.92 (48.32 to 65.53)		
2-Year Teff-high WT (Arm A n=75; Arm C n=49)	46.01 (38.36 to 53.66)	38.74 (30.26 to 47.22)		
1-Year ITT-WT (Arm A n=222; Arm C n=1972)	64.06 (59.02 to 69.11)	59.89 (54.61 to 65.17)		
2-Year ITT-WT (Arm A n=143; Arm C n=104)	41.45 (36.26 to 46.64)	31.79 (26.75 to 36.82)		

Statistical analyses

Statistical analysis title	OS Rate at Year 1

Statistical analysis description:

1-Year ITT-WT Population

Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	superiority[26]
P-value	= 0.2624
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	4.18

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.13
upper limit	11.48

Notes:

[26] - Stratified Analysis

Statistical analysis title	OS Rate at Year 2
Statistical analysis description:	
2-Year ITT-WT Population	
Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	= 0.0088
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	9.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.43
upper limit	16.9

Notes:

[27] - Stratified Analysis

Statistical analysis title	OS Rate at Year 1
Statistical analysis description:	
1-Year Teff-high WT Population	
Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	superiority[28]
P-value	= 0.0649
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	10.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	21.77

Notes:

[28] - Stratified Analysis

Statistical analysis title	OS Rate at Year 2

Statistical analysis description:	
2-Year Teff-high WT Population	
Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	= 0.212
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	7.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.15
upper limit	18.69

Notes:

[29] - Stratified Analysis

Secondary: Time to Deterioration (TTD) in Patient-Reported Lung Cancer Symptoms Determined by European Organization for Research and Treatment of Cancer (EORTC) Quality-of-Life Questionnaire-Core 30 (QLQ-C30) Score

End point title	Time to Deterioration (TTD) in Patient-Reported Lung Cancer Symptoms Determined by European Organization for Research and Treatment of Cancer (EORTC) Quality-of-Life Questionnaire-Core 30 (QLQ-C30) Score

End point description:

EORTC QLQ-C30 is a validated & reliable self-report measure that consists of 30 questions that assess 5 aspects of patient functioning, 3 symptom scales, health/quality of life,and 6 single items. EORTC QLQ-C30 is scored according to the EORTC scoring manual. All EORTC scales and single-item measures are linearly transformed so that each score has a range of 0-100. A high score for a functional/global health status scale represents a high or healthy level of functioning/HRQoL;however a high score for a symptom scale or item represents a high level of symptomatology or problems. A ≥10-point change in the symptoms subscale score is perceived by patients as clinically significant (Osoba et al.1998). Dyspnea in Teff-high WT (Arm A n=161; Arm B n=155; Arm C n= 129). Dyspnea ITT-WT (Arm A n=348; Arm B n=356; Arm C n= 336) Note: 999999=not estimable

End point type	Secondary

End point timeframe:

Baseline up to approximately 29 months

End point values	Arm C (Bevacizumab +Paclitaxel+Carboplatin)	Arm A (Atezolizumab +Paclitaxel+Carboplatin)	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	336	348	356	
Units: Months				
median (confidence interval 95%)				
Dyspnea in Teff-high WT	999999 (999999 to 999999)	999999 (999999 to 999999)	999999 (999999 to 999999)	

Dyspnea ITT-WT	999999 (999999 to 999999)	999999 (999999 to 999999)	999999 (999999 to 999999)	

Statistical analyses

Statistical analysis title	TTD EORTC QLQ-C30 Score
Statistical analysis description:	
Teff-high WT Population	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[30]
P-value	= 0.6899
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.909
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.571
upper limit	1.45

Notes:

[30] - Stratified Analysis

Statistical analysis title	TTD EORTC QLQ-C30 Score
Statistical analysis description:	
Teff-high WT Population	
Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	= 0.1043
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.671
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.413
upper limit	1.089

Notes:

[31] - Stratified Analysis

Statistical analysis title	TTD EORTC QLQ-C30 Score
Statistical analysis description:	
ITT WT	

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[32]
P-value	= 0.173
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.232
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.912
upper limit	1.665

Notes:

[32] - Stratified Analysis

Statistical analysis title	TTD EORTC QLQ-C30 Score

Statistical analysis description:

ITT WT

Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	superiority[33]
P-value	= 0.6145
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.084
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.792
upper limit	1.483

Notes:

[33] - Stratified Analysis

Secondary: TTD in Patient-Reported Lung Cancer Symptoms as Determined by EORTC Quality-of-Life Questionnaire-Core Lung Cancer Module 13 (QLQ-LC13) Score

End point title	TTD in Patient-Reported Lung Cancer Symptoms as Determined by EORTC Quality-of-Life Questionnaire-Core Lung Cancer Module 13 (QLQ-LC13) Score

End point description:

QLQ-LC13 incorporates 1 multiple-item scale & a series of single items.EORTC scales & single-item measures are linearly transformed so that each score has a range of 0-100.A high score for a functional/global health status scale represents a high or healthy level of functioning/HRQoL;a high score for a symptom scale or item represents a high level of symptomatology or problems.Cough in Teff-high WT(Arm A n=161;Arm B n=155;Arm C n=129).Dyspnea in Teff-high WT(Arm A n=161;Arm B n=155;Arm C n=129).Chest Pain in Teff-high WT (Arm A n=161;Arm B n=155;Arm C n=129).Arm and/or Shoulder Pain in Teff-high WT (Arm A n=161;Arm B n=155; Arm C n=129).Cough in ITT-WT(Arm A n=348;Arm B n=356;Arm C n=336).Dyspnea in ITT-WT (Arm A n=348; Arm B n=356;Arm C n=336).Arm and/or Shoulder Pain in ITT-WT(Arm A n=348;Arm B n=356;Arm C n=336).Pain in Chest in ITT-WT(Arm A n=348;Arm B n=356;Arm C n=336).Note: 999999=not estimable

End point type	Secondary

End point timeframe:

Baseline up to approximately 29 months

End point values	Arm C (Bevacizumab +Paclitaxel+Carboplatin)	Arm A (Atezolizumab +Paclitaxel+Carboplatin)	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	336	348	356	
Units: Months				
median (confidence interval 95%)				
Cough in Teff-high WT	999999 (999999 to 999999)	999999 (999999 to 999999)	999999 (21.0 to 999999)	
Dyspnea in Teff-high WT	999999 (6.3 to 999999)	999999 (5.6 to 999999)	999999 (999999 to 999999)	
Chest Pain in Teff-high WT	18.4 (18.4 to 999999)	999999 (999999 to 999999)	22.2 (22.2 to 999999)	
Arm and/or Shoulder Pain in Teff-high WT	999999 (12.7 to 999999)	999999 (18.3 to 999999)	19.5 (12.5 to 999999)	
Cough in ITT-WT	999999 (999999 to 999999)	999999 (999999 to 999999)	999999 (21.0 to 999999)	
Dyspnea in ITT-WT	999999 (10.0 to 999999)	21.9 (9.7 to 999999)	999999 (999999 to 999999)	
Arm and/or Shoulder Pain in ITT-WT	999999 (999999 to 999999)	999999 (18.3 to 999999)	19.5 (15.2 to 999999)	
Pain in Chest in ITT-WT	999999 (18.4 to 999999)	999999 (999999 to 999999)	999999 (22.2 to 999999)	

Statistical analyses

Statistical analysis title	TTD by EORTC QLQ-LC13 Score
Statistical analysis description: Cough for Teff-high WT ITT population	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[34]
P-value	= 0.8816
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.041

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.614
upper limit	1.763

Notes:

[34] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score
Statistical analysis description:	
Cough for Teff-high WT ITT Population	
Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	superiority[35]
P-value	= 0.2995
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.741
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.419
upper limit	1.309

Notes:

[35] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score
Statistical analysis description:	
Dyspnea in Teff-high WT Population	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[36]
P-value	= 0.7578
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.936
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.616
upper limit	1.422

Notes:

[36] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score

Statistical analysis description:	
Dyspnea in Teff-high WT Population	
Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	superiority[37]
P-value	= 0.847
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.041
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.694
upper limit	1.56

Notes:

[37] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score
Statistical analysis description:	
Pain in Chest in Teff-high WT Population	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[38]
P-value	= 0.1289
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.659
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.383
upper limit	1.133

Notes:

[38] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score
Statistical analysis description:	
Pain in Chest in Teff-high WT Population	
Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	superiority[39]
P-value	= 0.2381
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.729

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.235

Notes:

[39] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score

Statistical analysis description:

Arm and/or Shoulder Pain in Teff-high WT

Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[40]
P-value	= 0.7163
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.685
upper limit	1.732

Notes:

[40] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score

Statistical analysis description:

Arm and/or Shoulder Pain in Teff-high WT

Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	superiority[41]
P-value	= 0.1502
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.693
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	1.145

Notes:

[41] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score

Statistical analysis description: Cough in ITT-WT Population	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[42]
P-value	= 0.9568
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.713
upper limit	1.43

Notes:

[42] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score
Statistical analysis description: Cough in ITT-WT Population	
Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	superiority[43]
P-value	= 0.5377
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.891
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.619
upper limit	1.284

Notes:

[43] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score
Statistical analysis description: Dyspnea in ITT-WT Population	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[44]
P-value	= 0.4012
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.893

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.685
upper limit	1.163

Notes:

[44] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score
Statistical analysis description:	
Dyspnea in ITT-WT Population	
Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	superiority[45]
P-value	= 0.7149
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.809
upper limit	1.363

Notes:

[45] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score
Statistical analysis description:	
Arm and/or Shoulder Pain in ITT-WT	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[46]
P-value	= 0.7126
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.057
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.786
upper limit	1.422

Notes:

[46] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score

Statistical analysis description:	
Arm and/or Shoulder Pain in ITT-WT	
Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	superiority[47]
P-value	= 0.6053
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.921
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.675
upper limit	1.258

Notes:

[47] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score
Statistical analysis description:	
Pain in Chest in ITT-WT Population	
Comparison groups	Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	692
Analysis specification	Pre-specified
Analysis type	superiority[48]
P-value	= 0.3134
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.829
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.576
upper limit	1.194

Notes:

[48] - Stratified Analysis

Statistical analysis title	TTD by EORTC QLQ-LC13 Score
Statistical analysis description:	
Pain in Chest in ITT-WT Population	
Comparison groups	Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin)
Number of subjects included in analysis	684
Analysis specification	Pre-specified
Analysis type	superiority[49]
P-value	= 0.6115
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.633
upper limit	1.309

Notes:

[49] - Stratified Analysis

Secondary: Change From Baseline in Patient-Reported Lung Cancer Symptoms Score Using the Symptoms in Lung Cancer (SILC) Scale

End point title	Change From Baseline in Patient-Reported Lung Cancer Symptoms Score Using the Symptoms in Lung Cancer (SILC) Scale

End point description:

The SILC scale was used to assess patient-reported severity of lung cancer symptoms (chest pain, dyspnea, and cough). The SILC scale is a 9-item content validated self-report measure of lung cancer symptoms. It measures severity of cough, dyspnea, and chest pain with a symptom severity score. The SILC questionnaire comprises three individual symptoms (dyspnea, cough, chest pain) and are scored at the individual symptom level, thus have a dyspnea score, chest pain score, and cough score. Each individual symptom score is calculated as the average of responses for the symptom items [e.g. Chest Pain Score=mean (item 1; item 2)]. An increase in score is suggestive of a worsening in symptomology (i.e. frequency or severity). A score change of ≥0.3 points for the dyspnea and cough symptom scores is considered to be clinically significant; whereas a score change of ≥0.5 points for the chest pain score is considered to be clinically significant. Note: 999999=not available.

End point type	Secondary

End point timeframe:

Baseline up to approximately 29 months

End point values	Arm A (Atezolizumab +Paclitaxel+Carboplatin)	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[50]	0[51]	0[52]	
Units: Months				
median (confidence interval 95%)				
Teff-high WT	(to)	(to)	(to)	
ITT WT	(to)	(to)	(to)	

Notes:

[50] - No analysis due to psychometric properties in NSCLC population are being determined & quality issue.

[51] - No analysis due to psychometric properties in NSCLC population are being determined & quality issue.

[52] - No analysis due to psychometric properties in NSCLC population are being determined & quality issue.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Adverse Events

End point title	Percentage of Participants With Adverse Events

End point description:

End point type	Secondary

End point timeframe:

Baseline up to approximately 63 months

End point values	Arm B	Arm A	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[53]	0[54]	0[55]	
Units: Percentage				

Notes:

[53] - This will be reported at the time of final results posting.

[54] - This will be reported at the time of final results posting.

[55] - This will be reported at the time of final results posting.

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

End point type	Secondary

End point timeframe:

Baseline up to approximately 29 months

End point values	Arm A (Atezolizumab +Paclitaxel+Carboplatin)	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	389	376		
Units: Percentage of Participants				
number (not applicable)	4.6	2.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) of Atezolizumab in Arm A and Arm B

End point title	Maximum Observed Serum Concentration (Cmax) of Atezolizumab in Arm A and Arm B

End point description:

The predose samples will be collected on the same day of treatment administration. The infusion duration of atezolizumab will be of 30-60 minutes.

End point type	Secondary

End point timeframe:

Day 1 of Cycle 1 and 3 (Cycle length=21 days)

End point values	Arm A (Atezolizumab +Paclitaxel+Carboplatin)	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	378	364		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (Arm A n=378, Arm B n=364)	410 (± 157)	414 (± 127)		
Cycle 3 Day 1 (Arm A n=310, Arm B n=302)	498 (± 160)	540 (± 198)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Serum Concentration (Cmin) of Atezolizumab Prior to Infusion in Arm A and Arm B

End point title	Minimum Observed Serum Concentration (Cmin) of Atezolizumab Prior to Infusion in Arm A and Arm B

End point description:

Note: 999999=not available

End point type	Secondary

End point timeframe:

Day 21 of Cycles 1, 2 3, and 7 (Cycle length=21 days)

End point values	Arm A (Atezolizumab +Paclitaxel+Carboplatin)	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	354	345		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 21 (Arm A n=354; Arm B n=345)	76.4 (± 37.7)	80.8 (± 41.4)		

Cycle 2 Day 21 (Arm A n=322; Arm B n=319)	119 (± 55.7)	130 (± 57.1)		
Cycle 3 Day 21 (Arm A n=312; Arm B n=307)	146 (± 58.9)	160 (± 102)		
Cycle 7 Day 21 (Arm A n=230; Arm B n=249)	219 (± 89.6)	220 (± 99.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations for Carboplatin in Arm A, Arm B, and Arm C

End point title	Plasma Concentrations for Carboplatin in Arm A, Arm B, and Arm C

End point description:

Note: 999999=not available. BEOI=Before end of infusion. AI=After infusion.

End point type	Secondary

End point timeframe:

Predose (same day of treatment administration), 5-10 minutes before end of carboplatin infusion, 1 h after carboplatin infusion (infusion duration=15 to 30 minutes) on D1 of Cy1,3 (Cycle length=21 days)

End point values	Arm A (Atezolizumab +Paclitaxel+Carboplatin)	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	35	24	
Units: ng/mL				
arithmetic mean (standard deviation)				
Cy1D1 Pre-dose (Arm A n=28;Arm B n=35;Arm C n=24)	999999 (± 999999)	999999 (± 999999)	999999 (± 999999)	
Cy1D1 BEOI (Arm A n=26;Arm B n=32;Arm C n=24)	18300 (± 9610)	18300 (± 11900)	17200 (± 9860)	
Cy1D1 AI (Arm A n=26;Arm B n=31;Arm C n=22)	11700 (± 5570)	13900 (± 14300)	10100 (± 5320)	
Cy2D21 (Arm A n=19;Arm B n=27;Arm C n=17)	176 (± 82.9)	190 (± 113)	143 (± 73.0)	
Cy3D1 BEOI (Arm A n=18;Arm B n=28;Arm C n=16)	20900 (± 8330)	18700 (± 9410)	20600 (± 12900)	
Cy3D1 AI (Arm A n=20;Arm B n=27;Arm C n=17)	11700 (± 6990)	12200 (± 7480)	10400 (± 4150)	

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentrations for Paclitaxel in Arm A, Arm B, and Arm C

End point title	Plasma Concentrations for Paclitaxel in Arm A, Arm B, and Arm

	C

End point description:

Note: 999999=not available. BEOI=Before end of infusion. AI=After infusion

End point type	Secondary

End point timeframe:

Predose (same day of treatment administration), 5-10 minutes before end of paclitaxel infusion, 1 h after paclitaxel infusion (infusion duration=3 h) on D1 of Cy1,3 (Cycle length=21 days)

End point values	Arm A (Atezolizumab +Paclitaxel+Carboplatin)	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	28	35	24	
Units: ng/mL				
arithmetic mean (standard deviation)				
Cy1D1 Pre-dose (Arm A n=28; Arm B n=35;Arm C n=24)	999999 (± 999999)	999999 (± 999999)	999999 (± 999999)	
Cy1D1 BEOI (Arm A n=26;Arm B n=34;Arm C n=24)	4850 (± 2800)	6440 (± 3640)	5560 (± 2590)	
Cy1D1 AI (Arm A n=27;Arm B n=32;Arm C n=23)	2300 (± 2790)	2490 (± 3020)	1980 (± 1780)	
Cy2D21 (Arm A n=2;Arm B n=3; Arm C n=0)	999999 (± 999999)	999999 (± 999999)	999999 (± 999999)	
Cy3D1 BEOI (Arm A n=19; Arm B n=25; Arm C n=16)	5810 (± 3610)	7810 (± 4510)	7810 (± 5160)	
Cy3D1 AI (Arm A n=19;Arm B n=27;Arm C n=17)	1800 (± 1660)	2990 (± 5830)	1930 (± 1380)	

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of Bevacizumab in Arm B and Arm C

End point title	Cmax of Bevacizumab in Arm B and Arm C

End point description:

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 and Cycle 3 Day 1 (Cycle length=21 days)

End point values	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	205	215		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (Arm A n=205; Arm C n=215)	329 (± 129)	323 (± 95.0)		
Cycle 3 Day 1 (Arm A n=154; Arm C n=168)	413 (± 126)	430 (± 123)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cmin of Bevacizumab in Arm B and Arm C

End point title	Cmin of Bevacizumab in Arm B and Arm C
End point description:	
Note: 999999=not available	
End point type	Secondary
End point timeframe:	
Cycle 1 Day 1 and Cycle 2 Day 21 (Cycle length=21 days)	

End point values	Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin)	Arm C (Bevacizumab +Paclitaxel+Carboplatin)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	325	348		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 (Arm A n=325; Arm B n=348)	999999 (± 999999)	999999 (± 999999)		
Cycle 2 Day 21 (Arm A n=280; Arm B n=316)	98.0 (± 50.9)	90.4 (± 36.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the first study drug to the data cutoff date 13 Sept 2019 (up to approximately 53 months)	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0
Reporting groups	
Reporting group title	Arm B
Reporting group description: Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin	
Reporting group title	Arm C
Reporting group description: Bevacizumab+Paclitaxel+Carboplatin	
Reporting group title	Arm A
Reporting group description: Atezolizumab+Paclitaxel+Carboplatin	

Serious adverse events	Arm B	Arm C	Arm A
Total subjects affected by serious adverse events			
subjects affected / exposed	187 / 393 (47.58%)	142 / 394 (36.04%)	169 / 400 (42.25%)
number of deaths (all causes)	272	301	275
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA GASTRIC			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-CELL LYMPHOMA			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLADDER TRANSITIONAL CELL CARCINOMA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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

MARROW HYPERPLASIA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
MENINGIOMA			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METASTASES TO MENINGES			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TUMOUR PAIN			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
TUMOUR PSEUDOPROGRESSION			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
ANEURYSM			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
AORTIC DISSECTION			
subjects affected / exposed	2 / 393 (0.51%)	0 / 394 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
ARTERIAL OCCLUSIVE DISEASE			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEEP VEIN THROMBOSIS			

subjects affected / exposed	2 / 393 (0.51%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC VASCULAR DISORDER			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMBOLISM			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMBOLISM VENOUS			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
HAEMATOMA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
HYPERTENSION			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	0 / 400 (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
HYPOTENSION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHOEDEMA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
ORTHOSTATIC HYPOTENSION			

subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL ARTERY THROMBOSIS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
PERIPHERAL ISCHAEMIA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL VASCULAR DISORDER			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
THROMBOSIS			
subjects affected / exposed	2 / 393 (0.51%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
VENOUS THROMBOSIS LIMB			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
VERTEBROPLASTY			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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 disorders and administration site conditions			

ASTHENIA			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATHETER SITE ERYTHEMA			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHEST PAIN			
subjects affected / exposed	4 / 393 (1.02%)	6 / 394 (1.52%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 4	1 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COMPLICATION ASSOCIATED WITH DEVICE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
DEATH			
subjects affected / exposed	2 / 393 (0.51%)	2 / 394 (0.51%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 1
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	2 / 393 (0.51%)	2 / 394 (0.51%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFUSION SITE EXTRAVASATION			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
MUCOSAL INFLAMMATION			

subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PAIN			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	7 / 393 (1.78%)	1 / 394 (0.25%)	6 / 400 (1.50%)
occurrences causally related to treatment / all	2 / 7	0 / 1	3 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
ANAPHYLACTIC REACTION			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DRUG HYPERSENSITIVITY			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERSENSITIVITY			
subjects affected / exposed	1 / 393 (0.25%)	2 / 394 (0.51%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			

ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	3 / 400 (0.75%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
BRONCHOSTENOSIS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	3 / 393 (0.76%)	2 / 394 (0.51%)	3 / 400 (0.75%)
occurrences causally related to treatment / all	1 / 3	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
COUGH			
subjects affected / exposed	3 / 393 (0.76%)	0 / 394 (0.00%)	0 / 400 (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
DYSPNOEA			
subjects affected / exposed	2 / 393 (0.51%)	6 / 394 (1.52%)	4 / 400 (1.00%)
occurrences causally related to treatment / all	1 / 2	1 / 6	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPISTAXIS			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMOPTYSIS			
subjects affected / exposed	8 / 393 (2.04%)	2 / 394 (0.51%)	3 / 400 (0.75%)
occurrences causally related to treatment / all	3 / 8	1 / 2	0 / 4
deaths causally related to treatment / all	3 / 3	0 / 1	0 / 1
HICCUPS			

subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
HYPOXIA			
subjects affected / exposed	2 / 393 (0.51%)	1 / 394 (0.25%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMMUNE-MEDIATED PNEUMONITIS			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
PLEURAL EFFUSION			
subjects affected / exposed	0 / 393 (0.00%)	2 / 394 (0.51%)	3 / 400 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURISY			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURITIC PAIN			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA ASPIRATION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
PNEUMONITIS			

subjects affected / exposed	7 / 393 (1.78%)	0 / 394 (0.00%)	8 / 400 (2.00%)
occurrences causally related to treatment / all	7 / 7	0 / 0	8 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMOTHORAX			
subjects affected / exposed	0 / 393 (0.00%)	2 / 394 (0.51%)	4 / 400 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	5 / 393 (1.27%)	8 / 394 (2.03%)	7 / 400 (1.75%)
occurrences causally related to treatment / all	2 / 5	5 / 8	0 / 7
deaths causally related to treatment / all	0 / 2	2 / 2	0 / 0
PULMONARY HAEMORRHAGE			
subjects affected / exposed	2 / 393 (0.51%)	4 / 394 (1.02%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	2 / 2	3 / 4	0 / 0
deaths causally related to treatment / all	2 / 2	2 / 2	0 / 0
PULMONARY NECROSIS			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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 OEDEMA			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
RESPIRATORY FAILURE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
ALCOHOL WITHDRAWAL SYNDROME			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANXIETY			

subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BIPOLAR DISORDER			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
CONFUSIONAL STATE			
subjects affected / exposed	1 / 393 (0.25%)	2 / 394 (0.51%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DELIRIUM			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DELUSION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
MENTAL STATUS CHANGES			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PSYCHOTIC DISORDER			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUICIDAL IDEATION			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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 LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD PRESSURE INCREASED			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL CONDITION ABNORMAL			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
HEPATIC ENZYME INCREASED			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
LIPASE INCREASED			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
NEUTROPHIL COUNT DECREASED			

subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
PLATELET COUNT DECREASED			
subjects affected / exposed	2 / 393 (0.51%)	2 / 394 (0.51%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSAMINASES INCREASED			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TROPONIN INCREASED			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
WEIGHT DECREASED			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	2 / 393 (0.51%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ACCIDENTAL OVERDOSE			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			
subjects affected / exposed	2 / 393 (0.51%)	0 / 394 (0.00%)	0 / 400 (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
FEMUR FRACTURE			

subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FRACTURE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
HIP FRACTURE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFUSION RELATED REACTION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	3 / 400 (0.75%)
occurrences causally related to treatment / all	1 / 1	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HUMERUS FRACTURE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
PROCEDURAL COMPLICATION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
PROCEDURAL PAIN			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
RIB FRACTURE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
SPINAL COMPRESSION FRACTURE			

subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STERNAL FRACTURE			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
WOUND COMPLICATION			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
Cardiac disorders			
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	2 / 393 (0.51%)	3 / 394 (0.76%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	1 / 2	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
ATRIAL FIBRILLATION			
subjects affected / exposed	2 / 393 (0.51%)	1 / 394 (0.25%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FLUTTER			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
ATRIOVENTRICULAR BLOCK SECOND DEGREE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
CARDIAC ARREST			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	1 / 1
CARDIAC FAILURE			

subjects affected / exposed	2 / 393 (0.51%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
LEFT VENTRICULAR DYSFUNCTION			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	3 / 3	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
MYOCARDIAL ISCHAEMIA			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDIAL EFFUSION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
PERICARDITIS			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
TACHYARRHYTHMIA			

subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
Nervous system disorders			
ATAXIA			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
CEREBRAL INFARCTION			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CEREBRAL ISCHAEMIA			
subjects affected / exposed	2 / 393 (0.51%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	5 / 393 (1.27%)	1 / 394 (0.25%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	3 / 5	1 / 1	0 / 2
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
COGNITIVE DISORDER			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEPRESSED LEVEL OF CONSCIOUSNESS			

subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
DIZZINESS			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIZZINESS POSTURAL			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
DYSAESTHESIA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
ENCEPHALOPATHY			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOCAL DYSCOGNITIVE SEIZURES			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
HAEMORRHAGE INTRACRANIAL			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
HEADACHE			
subjects affected / exposed	2 / 393 (0.51%)	0 / 394 (0.00%)	0 / 400 (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
ISCHAEMIC STROKE			

subjects affected / exposed	1 / 393 (0.25%)	4 / 394 (1.02%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 1	3 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METABOLIC ENCEPHALOPATHY			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	0 / 400 (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
PARTIAL SEIZURES			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	0 / 393 (0.00%)	2 / 394 (0.51%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME			
subjects affected / exposed	0 / 393 (0.00%)	2 / 394 (0.51%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
PRESYNCOPE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
SEIZURE			

subjects affected / exposed	5 / 393 (1.27%)	1 / 394 (0.25%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	1 / 5	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SOMNOLENCE			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL CORD COMPRESSION			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYNCOPE			
subjects affected / exposed	1 / 393 (0.25%)	2 / 394 (0.51%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	2 / 393 (0.51%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	5 / 393 (1.27%)	4 / 394 (1.02%)	5 / 400 (1.25%)
occurrences causally related to treatment / all	5 / 5	4 / 4	5 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE MARROW FAILURE			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	0 / 400 (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
FEBRILE NEUTROPENIA			
subjects affected / exposed	27 / 393 (6.87%)	17 / 394 (4.31%)	13 / 400 (3.25%)
occurrences causally related to treatment / all	28 / 30	16 / 18	13 / 13
deaths causally related to treatment / all	3 / 3	0 / 0	0 / 0
LEUKOPENIA			

subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
NEUTROPENIA			
subjects affected / exposed	4 / 393 (1.02%)	2 / 394 (0.51%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	4 / 4	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NORMOCHROMIC ANAEMIA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
PANCYTOPENIA			
subjects affected / exposed	1 / 393 (0.25%)	3 / 394 (0.76%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	1 / 1	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPONTANEOUS HAEMATOMA			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOCYTOPENIA			
subjects affected / exposed	6 / 393 (1.53%)	2 / 394 (0.51%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	6 / 6	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
OPTIC NEUROPATHY			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 393 (0.25%)	3 / 394 (0.76%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	1 / 1	1 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN LOWER			

subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
COLITIS			
subjects affected / exposed	6 / 393 (1.53%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	5 / 6	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COLITIS ISCHAEMIC			
subjects affected / exposed	1 / 393 (0.25%)	2 / 394 (0.51%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONSTIPATION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	10 / 393 (2.54%)	3 / 394 (0.76%)	8 / 400 (2.00%)
occurrences causally related to treatment / all	6 / 11	3 / 3	7 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULAR PERFORATION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DUODENAL ULCER			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
DYSPHAGIA			

subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FAECALOMA			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
FOOD POISONING			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRIC HAEMORRHAGE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
GASTRITIS			
subjects affected / exposed	4 / 393 (1.02%)	0 / 394 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GLOSSODYNIA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
ILEUS PARALYTIC			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
INGUINAL HERNIA			

subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
INTESTINAL ANGINA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
INTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
INTESTINAL INFARCTION			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL ISCHAEMIA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
INTESTINAL PERFORATION			
subjects affected / exposed	0 / 393 (0.00%)	2 / 394 (0.51%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	2 / 2	0 / 0
IRRITABLE BOWEL SYNDROME			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
LARGE INTESTINAL HAEMORRHAGE			

subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
LARGE INTESTINE PERFORATION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
NAUSEA			
subjects affected / exposed	7 / 393 (1.78%)	3 / 394 (0.76%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	6 / 7	3 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OESOPHAGEAL FOOD IMPACTION			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	5 / 393 (1.27%)	3 / 394 (0.76%)	4 / 400 (1.00%)
occurrences causally related to treatment / all	4 / 5	3 / 3	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLANGITIS			
subjects affected / exposed	3 / 393 (0.76%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLANGITIS ACUTE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
CHOLELITHIASIS			

subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATITIS			
subjects affected / exposed	2 / 393 (0.51%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATOMEGALY			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATOTOXICITY			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
Skin and subcutaneous tissue disorders			
DERMATITIS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ERYTHEMA MULTIFORME			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	3 / 400 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PEMPHIGOID			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	3 / 400 (0.75%)
occurrences causally related to treatment / all	2 / 2	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			

subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	3 / 393 (0.76%)	3 / 394 (0.76%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	2 / 3	1 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GLOMERULONEPHROPATHY			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
HAEMATURIA			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
NEPHROLITHIASIS			
subjects affected / exposed	2 / 393 (0.51%)	0 / 394 (0.00%)	0 / 400 (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
PRERENAL FAILURE			
subjects affected / exposed	2 / 393 (0.51%)	0 / 394 (0.00%)	0 / 400 (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
RENAL FAILURE			
subjects affected / exposed	3 / 393 (0.76%)	0 / 394 (0.00%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL IMPAIRMENT			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL INJURY			

subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
TUBULOINTERSTITIAL NEPHRITIS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT OBSTRUCTION			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
ADRENAL INSUFFICIENCY			
subjects affected / exposed	2 / 393 (0.51%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	2 / 2	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ADRENOCORTICAL INSUFFICIENCY ACUTE			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETES INSIPIDUS			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOPHYSITIS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
HYPOTHYROIDISM			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION			

subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
SECONDARY ADRENOCORTICAL INSUFFICIENCY			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 1	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACK PAIN			
subjects affected / exposed	2 / 393 (0.51%)	3 / 394 (0.76%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 2	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE PAIN			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
COMPARTMENT SYNDROME			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
FLANK PAIN			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCULOSKELETAL CHEST PAIN			

subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYALGIA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
OSTEOLYSIS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SOFT TISSUE NECROSIS			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL PAIN			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VERTEBRAL FORAMINAL STENOSIS			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABDOMINAL SEPSIS			

subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL ABSCESS			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERAEMIA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BACTERIAL INFECTION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
BONE ABSCESS			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
BRONCHITIS			
subjects affected / exposed	3 / 393 (0.76%)	2 / 394 (0.51%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BURSITIS INFECTIVE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
CELLULITIS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
CHRONIC SINUSITIS			

subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIVERTICULITIS			
subjects affected / exposed	1 / 393 (0.25%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EMPYEMA			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENCEPHALITIS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOCARDITIS BACTERIAL			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTERITIS INFECTIOUS			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
ENTEROCOLITIS BACTERIAL			

subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
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 INFECTION			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS CLOSTRIDIAL			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMORRHAGIC PNEUMONIA			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
HEPATITIS A			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
HEPATITIS C			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
HERPES ZOSTER			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTED SKIN ULCER			

subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
INFECTION			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTIOUS PLEURAL EFFUSION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KLEBSIELLA SEPSIS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
LARGE INTESTINE INFECTION			
subjects affected / exposed	2 / 393 (0.51%)	0 / 394 (0.00%)	0 / 400 (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
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	3 / 400 (0.75%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG INFECTION			

subjects affected / exposed	2 / 393 (0.51%)	1 / 394 (0.25%)	4 / 400 (1.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC SEPSIS			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OSTEOMYELITIS			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
PAROTITIS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
PNEUMONIA			
subjects affected / exposed	26 / 393 (6.62%)	17 / 394 (4.31%)	17 / 400 (4.25%)
occurrences causally related to treatment / all	7 / 28	3 / 18	4 / 19
deaths causally related to treatment / all	0 / 1	1 / 3	0 / 2
PNEUMONIA ADENOVIRAL			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA BACTERIAL			
subjects affected / exposed	3 / 393 (0.76%)	0 / 394 (0.00%)	0 / 400 (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
PROSTATIC ABSCESS			

subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
PYOPNEUMOTHORAX			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
RESPIRATORY SYNCYTIAL VIRUS BRONCHITIS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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 SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	4 / 393 (1.02%)	2 / 394 (0.51%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	2 / 4	0 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
RESPIRATORY TRACT INFECTION FUNGAL			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
SALMONELLOSIS			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SCROTAL ABSCESS			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
SEPSIS			

subjects affected / exposed	3 / 393 (0.76%)	5 / 394 (1.27%)	3 / 400 (0.75%)
occurrences causally related to treatment / all	1 / 4	1 / 5	1 / 3
deaths causally related to treatment / all	0 / 0	1 / 2	0 / 1
SEPTIC SHOCK			
subjects affected / exposed	2 / 393 (0.51%)	0 / 394 (0.00%)	2 / 400 (0.50%)
occurrences causally related to treatment / all	1 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STAPHYLOCOCCAL BACTERAEMIA			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (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
TOOTH ABSCESS			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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 / 393 (0.25%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	3 / 393 (0.76%)	2 / 394 (0.51%)	4 / 400 (1.00%)
occurrences causally related to treatment / all	1 / 3	1 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASCULAR DEVICE INFECTION			
subjects affected / exposed	2 / 393 (0.51%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIRAL INFECTION			

subjects affected / exposed	3 / 393 (0.76%)	0 / 394 (0.00%)	0 / 400 (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
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	2 / 393 (0.51%)	0 / 394 (0.00%)	0 / 400 (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
DEHYDRATION			
subjects affected / exposed	7 / 393 (1.78%)	6 / 394 (1.52%)	3 / 400 (0.75%)
occurrences causally related to treatment / all	7 / 9	3 / 6	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FAILURE TO THRIVE			
subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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
HYPERCALCAEMIA			
subjects affected / exposed	0 / 393 (0.00%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 393 (0.00%)	1 / 394 (0.25%)	0 / 400 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOKALAEMIA			
subjects affected / exposed	2 / 393 (0.51%)	0 / 394 (0.00%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			
subjects affected / exposed	2 / 393 (0.51%)	1 / 394 (0.25%)	1 / 400 (0.25%)
occurrences causally related to treatment / all	0 / 2	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOPHOSPHATAEMIA			

subjects affected / exposed	1 / 393 (0.25%)	0 / 394 (0.00%)	0 / 400 (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

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

Non-serious adverse events	Arm B	Arm C	Arm A
Total subjects affected by non-serious adverse events			
subjects affected / exposed	375 / 393 (95.42%)	381 / 394 (96.70%)	385 / 400 (96.25%)
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	103 / 393 (26.21%)	87 / 394 (22.08%)	16 / 400 (4.00%)
occurrences (all)	147	102	16
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	84 / 393 (21.37%)	80 / 394 (20.30%)	75 / 400 (18.75%)
occurrences (all)	143	107	122
CHEST PAIN			
subjects affected / exposed	35 / 393 (8.91%)	28 / 394 (7.11%)	38 / 400 (9.50%)
occurrences (all)	37	32	45
FATIGUE			
subjects affected / exposed	136 / 393 (34.61%)	107 / 394 (27.16%)	110 / 400 (27.50%)
occurrences (all)	156	125	127
MALAISE			
subjects affected / exposed	27 / 393 (6.87%)	12 / 394 (3.05%)	21 / 400 (5.25%)
occurrences (all)	43	14	28
MUCOSAL INFLAMMATION			
subjects affected / exposed	37 / 393 (9.41%)	24 / 394 (6.09%)	10 / 400 (2.50%)
occurrences (all)	41	27	10
OEDEMA PERIPHERAL			
subjects affected / exposed	34 / 393 (8.65%)	19 / 394 (4.82%)	29 / 400 (7.25%)
occurrences (all)	41	20	33
PAIN			
subjects affected / exposed	26 / 393 (6.62%)	17 / 394 (4.31%)	22 / 400 (5.50%)
occurrences (all)	31	17	23
PYREXIA			

subjects affected / exposed	67 / 393 (17.05%)	34 / 394 (8.63%)	52 / 400 (13.00%)
occurrences (all)	88	44	63
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	85 / 393 (21.63%)	77 / 394 (19.54%)	81 / 400 (20.25%)
occurrences (all)	104	94	95
DYSPHONIA			
subjects affected / exposed	27 / 393 (6.87%)	18 / 394 (4.57%)	11 / 400 (2.75%)
occurrences (all)	27	19	12
DYSPNOEA			
subjects affected / exposed	66 / 393 (16.79%)	60 / 394 (15.23%)	85 / 400 (21.25%)
occurrences (all)	79	66	105
EPISTAXIS			
subjects affected / exposed	67 / 393 (17.05%)	86 / 394 (21.83%)	17 / 400 (4.25%)
occurrences (all)	88	108	22
HAEMOPTYSIS			
subjects affected / exposed	21 / 393 (5.34%)	18 / 394 (4.57%)	15 / 400 (3.75%)
occurrences (all)	24	21	26
OROPHARYNGEAL PAIN			
subjects affected / exposed	22 / 393 (5.60%)	10 / 394 (2.54%)	9 / 400 (2.25%)
occurrences (all)	25	10	10
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	31 / 393 (7.89%)	22 / 394 (5.58%)	21 / 400 (5.25%)
occurrences (all)	31	23	21
DEPRESSION			
subjects affected / exposed	25 / 393 (6.36%)	12 / 394 (3.05%)	15 / 400 (3.75%)
occurrences (all)	26	12	15
INSOMNIA			
subjects affected / exposed	41 / 393 (10.43%)	38 / 394 (9.64%)	50 / 400 (12.50%)
occurrences (all)	42	41	56
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	30 / 393 (7.63%)	20 / 394 (5.08%)	23 / 400 (5.75%)
occurrences (all)	44	24	27
ASPARTATE AMINOTRANSFERASE			

INCREASED			
subjects affected / exposed	30 / 393 (7.63%)	18 / 394 (4.57%)	22 / 400 (5.50%)
occurrences (all)	47	19	29
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	49 / 393 (12.47%)	34 / 394 (8.63%)	33 / 400 (8.25%)
occurrences (all)	86	72	64
PLATELET COUNT DECREASED			
subjects affected / exposed	57 / 393 (14.50%)	44 / 394 (11.17%)	40 / 400 (10.00%)
occurrences (all)	84	76	58
WEIGHT DECREASED			
subjects affected / exposed	52 / 393 (13.23%)	42 / 394 (10.66%)	27 / 400 (6.75%)
occurrences (all)	56	46	30
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	26 / 393 (6.62%)	20 / 394 (5.08%)	17 / 400 (4.25%)
occurrences (all)	42	39	27
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	27 / 393 (6.87%)	26 / 394 (6.60%)	27 / 400 (6.75%)
occurrences (all)	33	31	38
DYSGEUSIA			
subjects affected / exposed	24 / 393 (6.11%)	19 / 394 (4.82%)	15 / 400 (3.75%)
occurrences (all)	27	24	16
HEADACHE			
subjects affected / exposed	70 / 393 (17.81%)	53 / 394 (13.45%)	41 / 400 (10.25%)
occurrences (all)	87	65	49
NEUROPATHY PERIPHERAL			
subjects affected / exposed	92 / 393 (23.41%)	67 / 394 (17.01%)	104 / 400 (26.00%)
occurrences (all)	105	77	116
PARAESTHESIA			
subjects affected / exposed	53 / 393 (13.49%)	44 / 394 (11.17%)	37 / 400 (9.25%)
occurrences (all)	59	50	42
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	65 / 393 (16.54%)	54 / 394 (13.71%)	58 / 400 (14.50%)
occurrences (all)	73	59	65
Blood and lymphatic system disorders			

ANAEMIA			
subjects affected / exposed	115 / 393 (29.26%)	104 / 394 (26.40%)	145 / 400 (36.25%)
occurrences (all)	133	124	182
LEUKOPENIA			
subjects affected / exposed	14 / 393 (3.56%)	14 / 394 (3.55%)	20 / 400 (5.00%)
occurrences (all)	20	17	35
NEUTROPENIA			
subjects affected / exposed	72 / 393 (18.32%)	70 / 394 (17.77%)	60 / 400 (15.00%)
occurrences (all)	111	107	85
THROMBOCYTOPENIA			
subjects affected / exposed	52 / 393 (13.23%)	45 / 394 (11.42%)	48 / 400 (12.00%)
occurrences (all)	73	64	77
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	36 / 393 (9.16%)	20 / 394 (5.08%)	28 / 400 (7.00%)
occurrences (all)	48	24	35
CONSTIPATION			
subjects affected / exposed	122 / 393 (31.04%)	92 / 394 (23.35%)	102 / 400 (25.50%)
occurrences (all)	151	115	126
DIARRHOEA			
subjects affected / exposed	124 / 393 (31.55%)	98 / 394 (24.87%)	81 / 400 (20.25%)
occurrences (all)	218	133	134
DRY MOUTH			
subjects affected / exposed	21 / 393 (5.34%)	6 / 394 (1.52%)	13 / 400 (3.25%)
occurrences (all)	23	6	16
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	20 / 393 (5.09%)	9 / 394 (2.28%)	11 / 400 (2.75%)
occurrences (all)	20	11	13
NAUSEA			
subjects affected / exposed	149 / 393 (37.91%)	124 / 394 (31.47%)	129 / 400 (32.25%)
occurrences (all)	223	177	207
STOMATITIS			
subjects affected / exposed	54 / 393 (13.74%)	24 / 394 (6.09%)	23 / 400 (5.75%)
occurrences (all)	72	30	27
VOMITING			

subjects affected / exposed	71 / 393 (18.07%)	67 / 394 (17.01%)	68 / 400 (17.00%)
occurrences (all)	99	105	91
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	188 / 393 (47.84%)	180 / 394 (45.69%)	180 / 400 (45.00%)
occurrences (all)	195	183	182
DRY SKIN			
subjects affected / exposed	29 / 393 (7.38%)	9 / 394 (2.28%)	23 / 400 (5.75%)
occurrences (all)	31	9	26
PRURITUS			
subjects affected / exposed	54 / 393 (13.74%)	25 / 394 (6.35%)	50 / 400 (12.50%)
occurrences (all)	70	27	68
RASH			
subjects affected / exposed	70 / 393 (17.81%)	28 / 394 (7.11%)	71 / 400 (17.75%)
occurrences (all)	90	34	94
Renal and urinary disorders			
PROTEINURIA			
subjects affected / exposed	79 / 393 (20.10%)	63 / 394 (15.99%)	9 / 400 (2.25%)
occurrences (all)	123	81	13
Endocrine disorders			
HYPOTHYROIDISM			
subjects affected / exposed	50 / 393 (12.72%)	13 / 394 (3.30%)	33 / 400 (8.25%)
occurrences (all)	56	13	39
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	108 / 393 (27.48%)	88 / 394 (22.34%)	94 / 400 (23.50%)
occurrences (all)	175	135	145
BACK PAIN			
subjects affected / exposed	56 / 393 (14.25%)	43 / 394 (10.91%)	50 / 400 (12.50%)
occurrences (all)	66	49	69
BONE PAIN			
subjects affected / exposed	23 / 393 (5.85%)	19 / 394 (4.82%)	16 / 400 (4.00%)
occurrences (all)	31	19	18
MUSCLE SPASMS			
subjects affected / exposed	20 / 393 (5.09%)	7 / 394 (1.78%)	10 / 400 (2.50%)
occurrences (all)	24	8	10

MUSCULOSKELETAL PAIN			
subjects affected / exposed	48 / 393 (12.21%)	36 / 394 (9.14%)	36 / 400 (9.00%)
occurrences (all)	58	39	43
MYALGIA			
subjects affected / exposed	68 / 393 (17.30%)	53 / 394 (13.45%)	66 / 400 (16.50%)
occurrences (all)	116	81	103
PAIN IN EXTREMITY			
subjects affected / exposed	49 / 393 (12.47%)	33 / 394 (8.38%)	44 / 400 (11.00%)
occurrences (all)	62	44	50
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	28 / 393 (7.12%)	16 / 394 (4.06%)	14 / 400 (3.50%)
occurrences (all)	37	17	15
NASOPHARYNGITIS			
subjects affected / exposed	25 / 393 (6.36%)	17 / 394 (4.31%)	31 / 400 (7.75%)
occurrences (all)	32	18	48
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	36 / 393 (9.16%)	16 / 394 (4.06%)	23 / 400 (5.75%)
occurrences (all)	52	20	42
URINARY TRACT INFECTION			
subjects affected / exposed	35 / 393 (8.91%)	28 / 394 (7.11%)	37 / 400 (9.25%)
occurrences (all)	55	37	50
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	117 / 393 (29.77%)	86 / 394 (21.83%)	100 / 400 (25.00%)
occurrences (all)	155	102	128
DEHYDRATION			
subjects affected / exposed	33 / 393 (8.40%)	15 / 394 (3.81%)	7 / 400 (1.75%)
occurrences (all)	42	16	7
HYPOKALAEMIA			
subjects affected / exposed	36 / 393 (9.16%)	16 / 394 (4.06%)	24 / 400 (6.00%)
occurrences (all)	47	18	30
HYPOMAGNESAEMIA			
subjects affected / exposed	55 / 393 (13.99%)	25 / 394 (6.35%)	37 / 400 (9.25%)
occurrences (all)	76	29	48
HYPONATRAEMIA			

subjects affected / exposed occurrences (all)	23 / 393 (5.85%) 32	17 / 394 (4.31%) 20	13 / 400 (3.25%) 14

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 November 2014	Protocol was amended to change test product MPDL3280A to atezolizumab.
31 May 2016	Protocol was amended to include additional secondary end point to evaluate efficacy of atezolizumab as measured by investigator-assessed time to response (TTR) accordinto RECIST v1.1 for the ITT population, the TC1/2/3 or IC1/2/3 population, and the TC2/3 or IC2/3 population.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported