Clinical trial results:
A Phase III, Multicenter, Randomised, Double-Blind, Placebo-Controlled Study of Atezolizumab (Anti-Pd-L1 Antibody) in Combination With Paclitaxel Compared With Placebo With Paclitaxel for Patients With Previously Untreated Inoperable Locally Advanced or Metastatic Triple Negative Breast Cancer

Summary

EudraCT number	2016-004024-29
Trial protocol	SK DE CZ GB GR FR ES HR IT
Global end of trial date	

Results information

Result version number	v1
This version publication date	26 November 2020
First version publication date	26 November 2020

Trial information

Trial identification

Sponsor protocol code	MO39196

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03125902
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	Medical Communications, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	Medical Communications, Hoffmann-La Roche, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	15 November 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 November 2019
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This Phase 3, multicenter, randomized, double-blind, placebo controlled study is designed to evaluate the efficacy, pharmacokinetics and safety of atezolizumab (MPDL3280A, an anti-programmed death-ligand 1 [PD-L1] antibody) administered in combination with paclitaxel compared with placebo in combination with paclitaxel in subjects with previously untreated, inoperable locally advanced or metastatic, histologically documented TNBC. Subjects are randomized in a 2:1 ratio to receive atezolizumab or placebo plus paclitaxel until disease progression or unacceptable toxicity or end of study, whichever occurs first. In addition, the Sponsor may decide to terminate the study at any time.

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the following:

● Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines

● Applicable ICH Good Clinical Practice (GCP) Guidelines

● Applicable laws and regulations

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 August 2017
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	Argentina: 15
Country: Number of subjects enrolled	Brazil: 44
Country: Number of subjects enrolled	Canada: 34
Country: Number of subjects enrolled	China: 131
Country: Number of subjects enrolled	Czechia: 11
Country: Number of subjects enrolled	Germany: 41
Country: Number of subjects enrolled	Spain: 20
Country: Number of subjects enrolled	France: 63
Country: Number of subjects enrolled	United Kingdom: 28
Country: Number of subjects enrolled	Greece: 7
Country: Number of subjects enrolled	Croatia: 3
Country: Number of subjects enrolled	India: 27
Country: Number of subjects enrolled	Israel: 26
Country: Number of subjects enrolled	Italy: 64
Country: Number of subjects enrolled	Japan: 18

Country: Number of subjects enrolled	Morocco: 9
Country: Number of subjects enrolled	Romania: 11
Country: Number of subjects enrolled	Russian Federation: 24
Country: Number of subjects enrolled	Slovakia: 9
Country: Number of subjects enrolled	Turkey: 31
Country: Number of subjects enrolled	United States: 25
Country: Number of subjects enrolled	Vietnam: 9
Country: Number of subjects enrolled	South Africa: 1
Worldwide total number of subjects	651
EEA total number of subjects	257

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)	498
From 65 to 84 years	152
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Recruitment period: 06-Jun-2017 to 11-Sep-2019

Pre-assignment

Screening details:

The target population included subjects with previously untreated inoperable locally advanced or metastatic TNBC.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo + Paclitaxel

Arm description:

Participants will receive placebo matching to atezolizumab via IV infusion on Days 1 and 15 (± 3 days) of every 28-day cycle along with paclitaxel administered at a dose of 90 mg/m^2 via IV infusion on Days 1, 8, and 15 of every 28-day cycle until disease progression or unacceptable toxicity.

Arm type	Active comparator
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo matching to atezolizumab will be administered via IV infusion on Days 1 and 15 (± 3 days) of every 28-day cycle.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel will be administered at a dose of 90 mg/m^2 via IV infusion on Days 1, 8, and 15 of every 28-day cycle

Arm title	Atezolizumab + Paclitaxel

Arm description:

Participants will receive atezolizumab at a dose of 840 milligrams (mg) via intravenous (IV) infusion on Days 1 and 15 (± 3 days) of every 28-day cycle along with paclitaxel administered at a dose of 90 mg per square meter (mg/m^2) via IV infusion on Days 1, 8, and 15 of every 28-day cycle until disease progression or unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: Paclitaxel will be administered at a dose of 90 mg/m^2 via IV infusion on Days 1, 8, and 15 of every 28-day cycle	
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	MPDL3280A, an engineered anti-PDL1 antibody
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Atezolizumab is administered at a dose of 840 mg via IV infusion on Days 1 and 15 (± 3 days) of every 28-day cycle.	

Number of subjects in period 1	Placebo + Paclitaxel	Atezolizumab + Paclitaxel
Started	220	431
Completed	0	0
Not completed	220	431
Adverse event, serious fatal	52	123
Physician decision	1	-
Consent withdrawn by subject	13	25
Mastectomy	-	1
Study is ongoing	153	282
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo + Paclitaxel
Reporting group description:	
Participants will receive placebo matching to atezolizumab via IV infusion on Days 1 and 15 (± 3 days) of every 28-day cycle along with paclitaxel administered at a dose of 90 mg/m^2 via IV infusion on Days 1, 8, and 15 of every 28-day cycle until disease progression or unacceptable toxicity.	
Reporting group title	Atezolizumab + Paclitaxel
Reporting group description:	
Participants will receive atezolizumab at a dose of 840 milligrams (mg) via intravenous (IV) infusion on Days 1 and 15 (± 3 days) of every 28-day cycle along with paclitaxel administered at a dose of 90 mg per square meter (mg/m^2) via IV infusion on Days 1, 8, and 15 of every 28-day cycle until disease progression or unacceptable toxicity.	

Reporting group values	Placebo + Paclitaxel	Atezolizumab + Paclitaxel	Total
Number of subjects	220	431	651
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	176	322	498
>=65 years	44	109	153
Age Continuous Units: Years			
arithmetic mean	52.7	54.8	
standard deviation	± 12.2	± 12.6	-
Sex: Female, Male Units: Participants			
Female	220	430	650
Male	0	1	1
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	66	123	189
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	10	21	31
White	128	246	374
More than one race	2	3	5
Unknown or Not Reported	14	37	51
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	23	44	67
Not Hispanic or Latino	174	332	506
Unknown or Not Reported	23	55	78

Subject analysis sets	
Subject analysis set title	Placebo and Paclitaxel
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants will receive placebo matching to atezolizumab via IV infusion on Days 1 and 15 (± 3 days) of every 28-day cycle along with paclitaxel administered at a dose of 90 mg/m^2 via IV infusion on Days 1, 8, and 15 of every 28-day cycle until disease progression or unacceptable toxicity.

Subject analysis set title	Atezolizumab and Paclitaxel
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants will receive atezolizumab at a dose of 840 milligrams (mg) via intravenous (IV) infusion on Days 1 and 15 (± 3 days) of every 28-day cycle along with paclitaxel administered at a dose of 90 mg per square meter (mg/m^2) via IV infusion on Days 1, 8, and 15 of every 28-day cycle until disease progression or unacceptable toxicity.

Subject analysis set title	Placebo and Paclitaxel: PD-L1-Positive Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in the ITT population whose PD-L1 status was IC1/2/3 at the time of randomization

Subject analysis set title	Atezolizumab and Paclitaxel: PD-L1-Positive Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in the ITT population whose PD-L1 status was IC1/2/3 at the time of randomization

Reporting group values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel	Placebo and Paclitaxel: PD-L1-Positive Population
Number of subjects	220	431	101
Age Categorical Units: Participants			
<=18 years	0	0	
Between 18 and 65 years	176	322	
>=65 years	44	109	
Age Continuous Units: Years			
arithmetic mean	52.7	54.8	
standard deviation	± 12.2	± 12.6	±
Sex: Female, Male Units: Participants			
Female	220	430	
Male	0	1	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	66	123	
Native Hawaiian or Other Pacific Islander	0	1	
Black or African American	10	21	
White	128	246	
More than one race	2	3	
Unknown or Not Reported	14	37	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	23	44	
Not Hispanic or Latino	174	332	
Unknown or Not Reported	23	55	

Reporting group values	Atezolizumab and Paclitaxel: PD-L1-		

	Positive Population		
Number of subjects	191		
Age Categorical Units: Participants			
<=18 years Between 18 and 65 years >=65 years			
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			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino Not Hispanic or Latino Unknown or Not Reported			

End points

End points reporting groups

Reporting group title	Placebo + Paclitaxel
Reporting group description:	
Participants will receive placebo matching to atezolizumab via IV infusion on Days 1 and 15 (± 3 days) of every 28-day cycle along with paclitaxel administered at a dose of 90 mg/m^2 via IV infusion on Days 1, 8, and 15 of every 28-day cycle until disease progression or unacceptable toxicity.	
Reporting group title	Atezolizumab + Paclitaxel
Reporting group description:	
Participants will receive atezolizumab at a dose of 840 milligrams (mg) via intravenous (IV) infusion on Days 1 and 15 (± 3 days) of every 28-day cycle along with paclitaxel administered at a dose of 90 mg per square meter (mg/m^2) via IV infusion on Days 1, 8, and 15 of every 28-day cycle until disease progression or unacceptable toxicity.	
Subject analysis set title	Placebo and Paclitaxel
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants will receive placebo matching to atezolizumab via IV infusion on Days 1 and 15 (± 3 days) of every 28-day cycle along with paclitaxel administered at a dose of 90 mg/m^2 via IV infusion on Days 1, 8, and 15 of every 28-day cycle until disease progression or unacceptable toxicity.	
Subject analysis set title	Atezolizumab and Paclitaxel
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Participants will receive atezolizumab at a dose of 840 milligrams (mg) via intravenous (IV) infusion on Days 1 and 15 (± 3 days) of every 28-day cycle along with paclitaxel administered at a dose of 90 mg per square meter (mg/m^2) via IV infusion on Days 1, 8, and 15 of every 28-day cycle until disease progression or unacceptable toxicity.	
Subject analysis set title	Placebo and Paclitaxel: PD-L1-Positive Population
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants in the ITT population whose PD-L1 status was IC1/2/3 at the time of randomization	
Subject analysis set title	Atezolizumab and Paclitaxel: PD-L1-Positive Population
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants in the ITT population whose PD-L1 status was IC1/2/3 at the time of randomization	

Primary: Progression-Free Survival (PFS) Assessed Using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) in the Subpopulation with Programmed Death-Ligand 1 (PD-L1)-Positive Tumour Status

End point title	Progression-Free Survival (PFS) Assessed Using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) in the Subpopulation with Programmed Death-Ligand 1 (PD-L1)-Positive Tumour Status
End point description:	
PFS is defined as the time from randomization to the first occurrence of PD, as determined by the investigator using RECIST v1.1, or death from any cause during the study, whichever occurs first. PD is defined as greater than or equal to (>/=) 20 percent (%) relative increase and >/=5 millimeter (mm) of absolute increase in the sum of diameters (SD) of target lesions (TLs), taking as reference the smallest SD recorded since treatment started, or appearance of 1 or more new lesions.	
End point type	Primary
End point timeframe:	
From Day 1 to disease progression (PD) or death from any cause, assessed up to end of study (up to approximately 40 months)	

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	101	191		
Units: Months				
median (confidence interval 95%)	5.72 (5.39 to 7.20)	5.95 (5.62 to 7.43)		

Statistical analyses

Statistical analysis title	Stratified Analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	292
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2032
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.12

Statistical analysis title	Unstratified Analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	292
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2601
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.14

Primary: Progression-Free Survival (PFS) Assessed Using Response Evaluation

Criteria in Solid Tumors Version 1.1 (RECIST v1.1) in the Intent-to-Treat (ITT) Population	
End point title	Progression-Free Survival (PFS) Assessed Using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) in the Intent-to-Treat (ITT) Population

End point description:

PFS is defined as the time from randomization to the first occurrence of PD, as determined by the investigator using RECIST v1.1, or death from any cause during the study, whichever occurs first. PD is defined as greater than or equal to (>/=) 20 percent (%) relative increase and >/=5 millimeter (mm) of absolute increase in the sum of diameters (SD) of target lesions (TLs), taking as reference the smallest SD recorded since treatment started, or appearance of 1 or more new lesions.

End point type	Primary

End point timeframe:

From Day 1 to disease progression (PD) or death from any cause, assessed up to end of study (up to approximately 40 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	220	431		
Units: Months				
median (confidence interval 95%)	5.55 (5.36 to 6.51)	5.68 (5.42 to 7.16)		

Statistical analyses

Statistical analysis title	Stratified Analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	651
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1343
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.05

Statistical analysis title	Unstratified Analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel

Number of subjects included in analysis	651
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1285
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.05

Secondary: Overall Survival (OS) in the PD-L1-Positive Subpopulation

End point title	Overall Survival (OS) in the PD-L1-Positive Subpopulation

End point description:

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

0000 = Data not available
9999= Data not available

End point type	Secondary

End point timeframe:

From Day 1 to death from any cause, assessed up to end of study (up to approximately 40 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	101	191		
Units: Months				
median (confidence interval 95%)	9999 (19.06 to 9999)	9999 (22.05 to 9999)		

Statistical analyses

Statistical analysis title	Stratified Analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	292
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.142
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.55

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	2.8

Statistical analysis title	Unstratified Analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	292
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1374
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	2.79

Secondary: Overall Survival (OS) in the ITT Population

End point title	Overall Survival (OS) in the ITT Population

End point description:

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

0000 = Data not available
9999= Data not available

End point type	Secondary

End point timeframe:

From Day 1 to death from any cause, assessed up to end of study (up to approximately 40 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	220	431		
Units: Months				
median (confidence interval 95%)	22.80 (19.06 to 9999)	18.07 (15.90 to 9999)		

Statistical analyses

Statistical analysis title	Stratified analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	651
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1097
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.82

Statistical analysis title	Unstratified analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	651
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1411
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.76

Secondary: Percentage of Participants Who are Alive at 12 and 18 Months	
End point title	Percentage of Participants Who are Alive at 12 and 18 Months
End point description:	

End point type	Secondary
End point timeframe:	
From Day 1 to death from any cause, assessed up to 12 and 18 months	

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	220	431		
Units: Percentage of Participants				
number (confidence interval 95%)				
12 months	74.86 (67.53 to 82.18)	68.32 (62.70 to 73.94)		
18 months	60.95 (50.53 to 71.38)	51.02 (43.65 to 58.38)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to deterioration (TTD) in Global Health Status/ Health Related Quality of Life (HRQoL) in the PRO Evaluable Population

End point title	Time to deterioration (TTD) in Global Health Status/ Health Related Quality of Life (HRQoL) in the PRO Evaluable Population

End point description:

Deterioration in Global Health Status/HRQoL is defined as a decrease of at least 10 points on the Global Health Status /HRQoL scale (comprised of 2 items: 29 and 30) of the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30). The 2 items use 7-point scale (1 = very poor to 7 = Excellent). Scores are averaged, transformed to 0-100 scale; where higher score=better level of functioning or greater degree of symptoms.

0000 = Data not available
9999= Data not available

End point type	Secondary

End point timeframe:

From Day 1 to deterioration, assessed up to end of study (up to approximately 40 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	205	383		
Units: Months				
median (confidence interval 95%)	17.35 (9.63 to 9999)	12.45 (9.69 to 9999)		

Statistical analyses

Statistical analysis title	Stratified analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel

Number of subjects included in analysis	588
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8435
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.3

Secondary: Percentage of Participants Who are Alive Without Progression Event at Month 12 Assessed Using RECIST v1.1

End point title	Percentage of Participants Who are Alive Without Progression Event at Month 12 Assessed Using RECIST v1.1

End point description:

PD is defined as >/=20% relative increase and >/=5 mm of absolute increase in the SD of TLs, taking as reference the smallest SD recorded since treatment started, or appearance of 1 or more new lesions.

End point type	Secondary

End point timeframe:

From Day 1 to PD or death from any cause, assessed up to 12 months

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	220	431		
Units: Percentage of Participants				
number (confidence interval 95%)	16.22 (10.18 to 22.26)	21.63 (16.74 to 26.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Objective Response Assessed Using RECIST v1.1 in the PD-L1+ Response-evaluable population (Confirmed)

End point title	Percentage of Participants With Objective Response Assessed Using RECIST v1.1 in the PD-L1+ Response-evaluable population (Confirmed)

End point description:

Objective response is defined as complete response (CR) or partial response (PR), as determined by the investigator using RECIST v1.1 criteria. CR is defined as the disappearance of all TLs and SA reduction to less than (<) 10mm for nodal TLs/ non-TLs. PR is defined as >/=30% decrease in SD of TLs, taking as reference the baseline SD. Response-evaluable population: subjects in the ITT population with measurable disease at baseline. Responses were confirmed after 8 weeks if within first 12 months or

after 12 weeks if later.

End point type	Secondary

End point timeframe:

From Day 1 to PD, assessed up to end of study (up to approximately 40 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	101	191		
Units: Percentage of Participants				
number (confidence interval 95%)	40.6 (30.93 to 50.82)	49.2 (41.92 to 56.53)		

Statistical analyses

Statistical analysis title	Stratified analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	292
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1526
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	2.37

Secondary: Percentage of Participants With Objective Response Assessed Using RECIST v1.1 in the Response-evaluable population (Unconfirmed)

End point title	Percentage of Participants With Objective Response Assessed Using RECIST v1.1 in the Response-evaluable population (Unconfirmed)

End point description:

Objective response is defined as complete response (CR) or partial response (PR), as determined by the investigator using RECIST v1.1 criteria. CR is defined as the disappearance of all TLs and SA reduction to less than (<) 10mm for nodal TLs/ non-TLs. PR is defined as >/=30% decrease in SD of TLs, taking as reference the baseline SD.

End point type	Secondary

End point timeframe:

From Day 1 to PD, assessed up to end of study (up to approximately 40 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	101	191		
Units: Percentage of Participants				
number (confidence interval 95%)	55.4 (45.22 to 65.34)	63.4 (56.09 to 70.19)		

Statistical analyses

Statistical analysis title	Stratified analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	292
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1834
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	2.31

Secondary: Percentage of Participants With Objective Response Assessed Using RECIST v1.1 in the Response-evaluable population (Confirmed)

End point title	Percentage of Participants With Objective Response Assessed Using RECIST v1.1 in the Response-evaluable population (Confirmed)

End point description:

Objective response is defined as complete response (CR) or partial response (PR), as determined by the investigator using RECIST v1.1 criteria. CR is defined as the disappearance of all TLs and SA reduction to less than (<) 10mm for nodal TLs/ non-TLs. PR is defined as >/=30% decrease in SD of TLs, taking as reference the baseline SD. subjects in the ITT population with measurable disease at baseline. Responses were confirmed after 8 weeks if within first 12 months or after 12 weeks if later.

End point type	Secondary

End point timeframe:

From Day 1 to PD, assessed up to end of study (up to approximately 40 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	219	431		
Units: Percentage of Participants				
number (confidence interval 95%)	32.4 (26.27 to 39.05)	39.9 (35.25 to 44.70)		

Statistical analyses

Statistical analysis title	Stratified analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	650
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0513
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	2.02

Secondary: Percentage of Participants With Objective Response Assessed Using RECIST v1.1 in the Response-Evaluable Population (Unconfirmed)

End point title	Percentage of Participants With Objective Response Assessed Using RECIST v1.1 in the Response-Evaluable Population (Unconfirmed)

End point description:

Objective response is defined as complete response (CR) or partial response (PR), as determined by the investigator using RECIST v1.1 criteria. CR is defined as the disappearance of all TLs and SA reduction to less than (<) 10mm for nodal TLs/ non-TLs. PR is defined as >/=30% decrease in SD of TLs, taking as reference the baseline SD.

End point type	Secondary

End point timeframe:

From Day 1 to PD, assessed up to end of study (up to approximately 40 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	219	431		
Units: Percentage of Participants				
number (confidence interval 95%)	47.5 (40.72 to 54.33)	53.6 (48.76 to 58.38)		

Statistical analyses

Statistical analysis title	Stratified analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	650
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1226
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.81

Secondary: Duration of Objective Response (DOR) Assessed Using RECIST v1.1 in Response-evaluable population (Unconfirmed)

End point title	Duration of Objective Response (DOR) Assessed Using RECIST v1.1 in Response-evaluable population (Unconfirmed)

End point description:

DOR is defined as the time period from the date of initial CR or PR until the date of PD or death from any cause, whichever occurs first. CR is defined as the disappearance of all TLs and SA reduction to <10mm for nodal TLs/ non-TLs. PR is defined as >/=30% decrease in SD of TLs, taking as reference the baseline SD. PD is defined as >/=20% relative increase and >/=5 mm of absolute increase in the SD of TLs, taking as reference the smallest SD recorded since treatment started, or appearance of 1 or more new lesions.

End point type	Secondary

End point timeframe:

From objective response to PD, assessed up to end of study (up to approximately 40 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	104	231		
Units: Months				
median (confidence interval 95%)	5.45 (4.67 to 6.31)	6.41 (5.55 to 7.39)		

Statistical analyses

Statistical analysis title	Unstratified Analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	335
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0641
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.02

Secondary: Percentage of Participants With Clinical Benefit Assessed Using RECIST v1.1 in Response evaluable population

End point title	Percentage of Participants With Clinical Benefit Assessed Using RECIST v1.1 in Response evaluable population

End point description:

Clinical benefit is defined as the achievement of CR, PR, or stable disease according to RECIST v1.1 that lasts for at least 6 months. CR is defined as the disappearance of all TLs and SA reduction to <10mm for nodal TLs/ non-TLs. PR is defined as >/=30% decrease in SD of TLs, taking as reference the baseline SD. PD is defined as >/=20% relative increase and >/=5 mm of absolute increase in the SD of TLs, taking as reference the smallest SD recorded since treatment started, or appearance of 1 or more new lesions. Stable disease is defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD taking as reference smallest SD since treatment started.

End point type	Secondary

End point timeframe:

From Day 1 to PD, assessed up to end of study (up to approximately 40 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	219	431		
Units: Percentage of Participants				
number (confidence interval 95%)	49.8 (42.96 to 56.59)	57.1 (52.25 to 61.80)		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Serum Concentration (Cmin) of Atezolizumab

End point title	Minimum Observed Serum Concentration (Cmin) of

	Atezolizumab

End point description:

End point type	Secondary

End point timeframe:

Pre-dose (0 hours) on Day 1 of Cycles 2-4 and at treatment discontinuation (TD), (approximately 9 months).

End point values	Atezolizumab and Paclitaxel			
Subject group type	Subject analysis set			
Number of subjects analysed	342			
Units: µg/mL				
arithmetic mean (standard deviation)				
C2D1 predose n=316	139 (± 53.3)			
C3D1 predose n=277	208 (± 78.3)			
C4D1 predose n=243	242 (± 84.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) of Atezolizumab

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

End point description:

End point type	Secondary

End point timeframe:

C1D1 30 min postdose

End point values	Atezolizumab and Paclitaxel			
Subject group type	Subject analysis set			
Number of subjects analysed	308			
Units: µg/mL				
arithmetic mean (standard deviation)	321 (± 90.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Plasma Concentration (Cmin) of Paclitaxel

End point title	Minimum Observed Plasma Concentration (Cmin) of Paclitaxel
End point description: 0000 = Data not available 9999= Data not available	
End point type	Secondary
End point timeframe: Pre-dose (0 hours) on Day 1 of Cycle 3 (1 Cycle = 28 days)	

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23	37		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	1.51 (± 9999)	1.67 (± 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Paclitaxel

End point title	Maximum Observed Plasma Concentration (Cmax) of Paclitaxel
End point description:	
End point type	Secondary
End point timeframe: Pre-dose (0 hours), 5-10 min before and after paclitaxel infusion, 60 min after paclitaxel infusion on Day 1 of Cycles 1 and 3 (paclitaxel infusion duration= 60 min) (1 Cycle = 28 days)	

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23	37		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
C1D1 Post-Dose (n= 23; n=37)	518 (± 290.7)	301 (± 1501)		
C3D1 Post-Dose (n=16; n=26)	666 (± 339)	276 (± 1360)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Adverse Events (AEs) and Serious AEs (SAEs)

End point title	Percentage of Participants With Adverse Events (AEs) and Serious AEs (SAEs)

End point description:

Investigator text for AEs is coded using MedDRA version 23.0

End point type	Secondary

End point timeframe:

From Day 1 to 90 days after last dose of study drug, assessed up to end of study (up to approximately 40 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	218	431		
Units: Percentage of participants				
number (not applicable)				
Percentage of participants with at least one AE	97.7	99.1		
Total number of participants with at least one SAE	16.1	22.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anti-Drug Antibodies (ADAs)

End point title	Percentage of Participants With Anti-Drug Antibodies (ADAs)

End point description:

End point type	Secondary

End point timeframe:

Pre-dose (0 hours) on Day 1 of Cycles 1, 2, 3, 4, 8, 12, 16, and at every 8 cycles thereafter until TD, at TD, and at 90-150 days after TD (maximum up to 45 months) (1 Cycle = 28 days)

End point values	Atezolizumab and Paclitaxel			
Subject group type	Subject analysis set			
Number of subjects analysed	334			
Units: Percentage of Participants				
number (not applicable)				
Positive for ADA at Baseline	1.5			
Positive for ADA Post-baseline	14.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival by PD-L1 Status, Intent to Treat Population

End point title	Overall Survival by PD-L1 Status, Intent to Treat Population

End point description:

ITT population: all randomized participants, whether or not the assigned study treatment was received

9999=Insufficient number of participants with events

End point type	Secondary

End point timeframe:

From Day 1 up to primary analysis (up to approximately 26 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	220	431		
Units: Months				
median (confidence interval 95%)				
PD-L1 IC0 (n= 119, n= 240)	20.37 (19.94 to 25.10)	16.26 (13.50 to 18.99)		
PD-L1 IC1/2/3 (n= 101, n=191)	9999 (19.06 to 9999)	9999 (22.05 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival by PD-L1 Status, Intent to Treat Population

End point title	Progression Free Survival by PD-L1 Status, Intent to Treat Population

End point description:

ITT population: all randomized participants, whether or not the assigned study treatment was received

End point type	Secondary

End point timeframe:

From Day 1 up to primary completion date (approximately 26 months)

End point values	Placebo + Paclitaxel	Atezolizumab + Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	431		
Units: Months				
median (confidence interval 95%)				
PD-L1 IC0 (n=119, n=240)	5.49 (3.84 to 6.51)	5.45 (4.60 to 6.51)		
PD-L1 IC1/2/3 (n=101, n=191)	5.72 (5.39 to 7.20)	5.95 (5.62 to 7.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Confirmed Response (C-DoR) in C-DoR Evaluable Population

End point title	Duration of Confirmed Response (C-DoR) in C-DoR Evaluable Population

End point description:

C-DoR is defined as the time from the first occurrence of a documented confirmed response (CR or PR) until the date of disease progression per RECIST v1.1 or death from any cause, whichever occurs first.

End point type	Secondary

End point timeframe:

From objective response to PD, assessed up to end of study (up to approximately 40 months)

End point values	Placebo and Paclitaxel	Atezolizumab and Paclitaxel		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	172		
Units: Months				
median (confidence interval 95%)	5.75 (5.36 to 7.56)	7.66 (7.16 to 11.33)		

Statistical analyses

Statistical analysis title	Unstratified Analysis
Comparison groups	Placebo and Paclitaxel v Atezolizumab and Paclitaxel
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.01227
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.62

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	0.9

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Day 1 to 90 days after last dose of study drug, assessed up to end of study (up to approximately 40 months)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Placebo + Paclitaxel

Reporting group description:

Participants will receive placebo matching to atezolizumab via IV infusion on Days 1 and 15 (± 3 days) of every 28-day cycle along with paclitaxel administered at a dose of 90 mg/m^2 via IV infusion on Days 1, 8, and 15 of every 28-day cycle until disease progression or unacceptable toxicity.

Reporting group title	Atezolizumab + Paclitaxel

Reporting group description:

Participants will receive atezolizumab at a dose of 840 milligrams (mg) via intravenous (IV) infusion on Days 1 and 15 (± 3 days) of every 28-day cycle along with paclitaxel administered at a dose of 90 mg per square meter (mg/m^2) via IV infusion on Days 1, 8, and 15 of every 28-day cycle until disease progression or unacceptable toxicity.

Serious adverse events	Placebo + Paclitaxel	Atezolizumab + Paclitaxel	
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 218 (16.06%)	98 / 431 (22.74%)	
number of deaths (all causes)	4	9	
number of deaths resulting from adverse events	0	4	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
METASTASES TO CENTRAL NERVOUS SYSTEM			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUMOUR PAIN			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
DEEP VEIN THROMBOSIS			

subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATOMA			
subjects affected / exposed	1 / 218 (0.46%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTENSIVE CRISIS			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTENSION			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOSIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
DEATH			
subjects affected / exposed	0 / 218 (0.00%)	3 / 431 (0.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	1 / 3	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
PYREXIA			

subjects affected / exposed	1 / 218 (0.46%)	3 / 431 (0.70%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
ANAPHYLACTIC REACTION			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
BREAST FIBROSIS			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPISTAXIS			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMOPTYSIS			

subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERSTITIAL LUNG DISEASE			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG DISORDER			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	0 / 218 (0.00%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS			
subjects affected / exposed	0 / 218 (0.00%)	6 / 431 (1.39%)	
occurrences causally related to treatment / all	0 / 0	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 218 (0.00%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY DISTRESS			
subjects affected / exposed	0 / 218 (0.00%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
DEPRESSION			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			

DEVICE BREAKAGE			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE KINK			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 218 (0.46%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSAMINASES INCREASED			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
COMPRESSION FRACTURE			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMUR FRACTURE			
subjects affected / exposed	0 / 218 (0.00%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFUSION RELATED REACTION			
subjects affected / exposed	2 / 218 (0.92%)	3 / 431 (0.70%)	
occurrences causally related to treatment / all	2 / 2	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCEDURAL PNEUMOTHORAX			

subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
CARDIAC FAILURE			
subjects affected / exposed	1 / 218 (0.46%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	1 / 1	
PERICARDITIS			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
CEREBRAL VENOUS SINUS THROMBOSIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COGNITIVE DISORDER			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPILEPSY			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

HEADACHE			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYASTHENIA GRAVIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SCIATICA			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEIZURE			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 218 (0.92%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	1 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
BICYTOPENIA			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BONE MARROW FAILURE			
subjects affected / exposed	1 / 218 (0.46%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE NEUTROPENIA			
subjects affected / exposed	1 / 218 (0.46%)	3 / 431 (0.70%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
LYMPHADENITIS			

subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
subjects affected / exposed	0 / 218 (0.00%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
KERATITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORBITAL MYOSITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

COLITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS ULCERATIVE			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	1 / 218 (0.46%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC ULCER			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL ULCER			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATEMESIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
IMMUNE-MEDIATED PANCREATITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			
subjects affected / exposed	0 / 218 (0.00%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS			

subjects affected / exposed	0 / 218 (0.00%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS ACUTE			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL HAEMORRHAGE			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	3 / 218 (1.38%)	3 / 431 (0.70%)	
occurrences causally related to treatment / all	1 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC FUNCTION ABNORMAL			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 218 (0.00%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
GLOMERULONEPHRITIS CHRONIC			

subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEPHRITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL IMPAIRMENT			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
HYPOPHYSITIS			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTHYROIDISM			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 218 (0.00%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

PATHOLOGICAL FRACTURE			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
POLYMYOSITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA INFECTIOUS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIVERTICULITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ERYSIPELAS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES ZOSTER			

subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			
subjects affected / exposed	2 / 218 (0.92%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYELITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMOCYSTIS JIROVECII PNEUMONIA			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	3 / 218 (1.38%)	9 / 431 (2.09%)	
occurrences causally related to treatment / all	0 / 3	3 / 9	
deaths causally related to treatment / all	0 / 2	0 / 0	
POSTOPERATIVE WOUND INFECTION			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY SEPSIS			

subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
PYELONEPHRITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	1 / 218 (0.46%)	4 / 431 (0.93%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 1	1 / 1	
SOFT TISSUE INFECTION			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STAPHYLOCOCCAL SKIN INFECTION			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TOOTH INFECTION			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 218 (0.46%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			

subjects affected / exposed	1 / 218 (0.46%)	3 / 431 (0.70%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR DEVICE INFECTION			
subjects affected / exposed	3 / 218 (1.38%)	2 / 431 (0.46%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
VESTIBULAR NEURONITIS			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
WOUND INFECTION			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIABETES MELLITUS			
subjects affected / exposed	1 / 218 (0.46%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERAMYLASAEMIA			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERLIPASAEMIA			

subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOCALCAEMIA			
subjects affected / exposed	1 / 218 (0.46%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPONATRAEMIA			
subjects affected / exposed	0 / 218 (0.00%)	1 / 431 (0.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOPROTEINAEMIA			
subjects affected / exposed	1 / 218 (0.46%)	0 / 431 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo + Paclitaxel	Atezolizumab + Paclitaxel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	209 / 218 (95.87%)	418 / 431 (96.98%)	
Vascular disorders			
HOT FLUSH			
subjects affected / exposed	11 / 218 (5.05%)	17 / 431 (3.94%)	
occurrences (all)	12	19	
HYPERTENSION			
subjects affected / exposed	11 / 218 (5.05%)	18 / 431 (4.18%)	
occurrences (all)	11	32	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	45 / 218 (20.64%)	99 / 431 (22.97%)	
occurrences (all)	59	139	
FATIGUE			

subjects affected / exposed	55 / 218 (25.23%)	117 / 431 (27.15%)	
occurrences (all)	68	148	
OEDEMA PERIPHERAL			
subjects affected / exposed	20 / 218 (9.17%)	42 / 431 (9.74%)	
occurrences (all)	27	55	
PYREXIA			
subjects affected / exposed	25 / 218 (11.47%)	62 / 431 (14.39%)	
occurrences (all)	33	83	
Reproductive system and breast disorders			
BREAST PAIN			
subjects affected / exposed	8 / 218 (3.67%)	26 / 431 (6.03%)	
occurrences (all)	8	31	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	35 / 218 (16.06%)	82 / 431 (19.03%)	
occurrences (all)	43	102	
DYSPNOEA			
subjects affected / exposed	24 / 218 (11.01%)	46 / 431 (10.67%)	
occurrences (all)	29	54	
EPISTAXIS			
subjects affected / exposed	15 / 218 (6.88%)	25 / 431 (5.80%)	
occurrences (all)	18	29	
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	21 / 218 (9.63%)	30 / 431 (6.96%)	
occurrences (all)	21	36	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	34 / 218 (15.60%)	79 / 431 (18.33%)	
occurrences (all)	53	138	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	38 / 218 (17.43%)	80 / 431 (18.56%)	
occurrences (all)	60	134	
NEUTROPHIL COUNT DECREASED			

subjects affected / exposed	33 / 218 (15.14%)	62 / 431 (14.39%)	
occurrences (all)	169	226	
WEIGHT DECREASED			
subjects affected / exposed	6 / 218 (2.75%)	27 / 431 (6.26%)	
occurrences (all)	6	28	
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	29 / 218 (13.30%)	60 / 431 (13.92%)	
occurrences (all)	165	190	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	18 / 218 (8.26%)	32 / 431 (7.42%)	
occurrences (all)	21	36	
DYSGEUSIA			
subjects affected / exposed	16 / 218 (7.34%)	32 / 431 (7.42%)	
occurrences (all)	18	34	
HEADACHE			
subjects affected / exposed	36 / 218 (16.51%)	51 / 431 (11.83%)	
occurrences (all)	41	64	
HYPOAESTHESIA			
subjects affected / exposed	14 / 218 (6.42%)	23 / 431 (5.34%)	
occurrences (all)	18	33	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	58 / 218 (26.61%)	117 / 431 (27.15%)	
occurrences (all)	80	154	
PARAESTHESIA			
subjects affected / exposed	22 / 218 (10.09%)	37 / 431 (8.58%)	
occurrences (all)	30	46	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	23 / 218 (10.55%)	41 / 431 (9.51%)	
occurrences (all)	26	49	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	60 / 218 (27.52%)	118 / 431 (27.38%)	
occurrences (all)	102	229	
LEUKOPENIA			

subjects affected / exposed	15 / 218 (6.88%)	49 / 431 (11.37%)	
occurrences (all)	32	148	
NEUTROPENIA			
subjects affected / exposed	46 / 218 (21.10%)	91 / 431 (21.11%)	
occurrences (all)	98	215	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	18 / 218 (8.26%)	34 / 431 (7.89%)	
occurrences (all)	20	39	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	14 / 218 (6.42%)	38 / 431 (8.82%)	
occurrences (all)	20	43	
CONSTIPATION			
subjects affected / exposed	31 / 218 (14.22%)	79 / 431 (18.33%)	
occurrences (all)	51	95	
DIARRHOEA			
subjects affected / exposed	48 / 218 (22.02%)	117 / 431 (27.15%)	
occurrences (all)	75	184	
DRY MOUTH			
subjects affected / exposed	7 / 218 (3.21%)	22 / 431 (5.10%)	
occurrences (all)	8	30	
DYSPEPSIA			
subjects affected / exposed	11 / 218 (5.05%)	16 / 431 (3.71%)	
occurrences (all)	12	17	
NAUSEA			
subjects affected / exposed	53 / 218 (24.31%)	111 / 431 (25.75%)	
occurrences (all)	92	155	
STOMATITIS			
subjects affected / exposed	10 / 218 (4.59%)	23 / 431 (5.34%)	
occurrences (all)	14	27	
VOMITING			
subjects affected / exposed	20 / 218 (9.17%)	66 / 431 (15.31%)	
occurrences (all)	34	102	
Skin and subcutaneous tissue disorders			
ALOPECIA			

subjects affected / exposed	116 / 218 (53.21%)	252 / 431 (58.47%)	
occurrences (all)	121	256	
ERYTHEMA			
subjects affected / exposed	6 / 218 (2.75%)	24 / 431 (5.57%)	
occurrences (all)	6	28	
PRURITUS			
subjects affected / exposed	18 / 218 (8.26%)	40 / 431 (9.28%)	
occurrences (all)	20	64	
RASH			
subjects affected / exposed	35 / 218 (16.06%)	73 / 431 (16.94%)	
occurrences (all)	51	98	
Endocrine disorders			
HYPERTHYROIDISM			
subjects affected / exposed	0 / 218 (0.00%)	22 / 431 (5.10%)	
occurrences (all)	0	25	
HYPOTHYROIDISM			
subjects affected / exposed	5 / 218 (2.29%)	43 / 431 (9.98%)	
occurrences (all)	5	49	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	14 / 218 (6.42%)	50 / 431 (11.60%)	
occurrences (all)	18	74	
BACK PAIN			
subjects affected / exposed	18 / 218 (8.26%)	38 / 431 (8.82%)	
occurrences (all)	21	42	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	9 / 218 (4.13%)	24 / 431 (5.57%)	
occurrences (all)	9	25	
MYALGIA			
subjects affected / exposed	23 / 218 (10.55%)	45 / 431 (10.44%)	
occurrences (all)	32	56	
PAIN IN EXTREMITY			
subjects affected / exposed	22 / 218 (10.09%)	45 / 431 (10.44%)	
occurrences (all)	33	55	
Infections and infestations			

NASOPHARYNGITIS			
subjects affected / exposed	16 / 218 (7.34%)	32 / 431 (7.42%)	
occurrences (all)	17	35	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	12 / 218 (5.50%)	24 / 431 (5.57%)	
occurrences (all)	14	33	
URINARY TRACT INFECTION			
subjects affected / exposed	10 / 218 (4.59%)	32 / 431 (7.42%)	
occurrences (all)	12	41	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	18 / 218 (8.26%)	63 / 431 (14.62%)	
occurrences (all)	27	100	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 May 2017	The protocol was amended to address regulatory requests for revisions as part of review through the Voluntary Harmonisation Procedure (VHP).
05 December 2017	The protocol was amended to include updated safety and efficacy data from the revised Investigator's Brochure (version 10), align screening assessments for hepatitis in inclusion vs. exclusion criteria across atezolizumab studies, reduce schedule for PK and ADA assessments, update select laboratory assessments in the China population, and to clarify acceptable assessment windows.
17 December 2018	The major changes to the protocol were prompted by the results of primary analysis of the IMpassion130 (WO29522) study.
23 May 2019	Key changes included: • Removal of a planned interim analysis of PFS at 80% information fraction in the PD-L1positive population as a result of feedback from the US Food and Drug Administration (FDA). • Adjustment of target number of primary endpoint events from 158 to 155 with the removal of interim analysis of PFS. • Addition of two new secondary endpoints in keeping with a request from the US FDA: confirmed objective response rate (C-ORR), and duration of confirmed response (C-DoR) • Addition of immune-mediated myositis to the list of identified risks for atezolizumab, along with management guidelines for this newly added risk. Requirements for permanent treatment discontinuation in case of immune-related myositis were clarified.
11 February 2020	This amendment included updates to risks and management guidelines that aligned with the latest atezolizumab IB (v15.0)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported