Clinical trial results:
A Phase III, Randomised, Double-blind, Placebo-controlled, Multicentre Study of the Efficacy and Safety of Atezolizumab Plus Chemotherapy for Patients With Early Relapsing Recurrent (Inoperable Locally Advanced or Metastatic) Triple-negative Breast Cancer

Summary

EudraCT number	2016-005119-42
Trial protocol	HU GB ES FR FI PL PT IT
Global end of trial date	23 October 2024

Results information

Result version number	v1 (current)
This version publication date	31 October 2025
First version publication date	31 October 2025

Trial information

Trial identification

Sponsor protocol code	MO39193

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03371017
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4058
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 October 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the efficacy and safety of atezolizumab plus chemotherapy compared with placebo plus chemotherapy in participants with inoperable locally advanced or metastatic triple-negative breast cancer (TNBC).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 January 2018
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: 2
Country: Number of subjects enrolled	Bosnia and Herzegovina: 4
Country: Number of subjects enrolled	Brazil: 36
Country: Number of subjects enrolled	Chile: 4
Country: Number of subjects enrolled	China: 70
Country: Number of subjects enrolled	Cuba: 3
Country: Number of subjects enrolled	Germany: 13
Country: Number of subjects enrolled	Spain: 43
Country: Number of subjects enrolled	Finland: 8
Country: Number of subjects enrolled	France: 57
Country: Number of subjects enrolled	United Kingdom: 34
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Italy: 70
Country: Number of subjects enrolled	Kazakhstan: 7
Country: Number of subjects enrolled	Korea, Republic of: 54
Country: Number of subjects enrolled	Morocco: 9
Country: Number of subjects enrolled	Mexico: 34
Country: Number of subjects enrolled	Montenegro: 1
Country: Number of subjects enrolled	Panama: 2
Country: Number of subjects enrolled	Peru: 2
Country: Number of subjects enrolled	Poland: 8

Country: Number of subjects enrolled	Portugal: 3
Country: Number of subjects enrolled	Russian Federation: 27
Country: Number of subjects enrolled	Singapore: 4
Country: Number of subjects enrolled	Serbia: 19
Country: Number of subjects enrolled	Türkiye: 55
Country: Number of subjects enrolled	United States: 9
Country: Number of subjects enrolled	South Africa: 8
Worldwide total number of subjects	595
EEA total number of subjects	211

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)	535
From 65 to 84 years	60
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 595 participants with inoperable locally advanced or metastatic TNBC took part in the study at 126 investigative sites in 28 countries from 11 January 2018 to 23 October 2024.

Pre-assignment

Screening details:

Participants were randomized in a 1:1 ratio to receive atezolizumab with chemotherapy or placebo with chemotherapy.

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, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo + Chemotherapy

Arm description:

Participants received atezolizumab matching placebo, by intravenous (IV) infusion on Day 1 of each cycle along with either gemcitabine, 1000 milligrams per square meter (mg/m^2), followed by carboplatin target under the curve (AUC) 2 milligrams per milliliter per minute (mg/ml/min), both administered by IV infusion on Days 1 and 8 of each cycle or capecitabine 1000 mg/m^2 , twice daily (BID), orally on Days 1 to 14, followed by a 7-day rest period in each cycle (1 Cycle= 3 weeks). Treatment was continued until disease progression (PD), unacceptable toxicity, death or participant or investigator decision to discontinue treatment.

Arm type	Placebo
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received carboplatin target AUC 2 mg/ml/min, administered by IV infusion on Days 1 and 8 of each cycle, followed by a 7-day rest period in each cycle (1 Cycle= 3 weeks).

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received capecitabine 1000 mg/m^2, BID, orally on Days 1 to 14, followed by a 7-day rest period in each cycle (1 Cycle= 3 weeks).

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received gemcitabine, 1000 mg/m^2, administered by IV infusion on Days 1 and 8 of each cycle, followed by a 7-day rest period in each cycle (1 Cycle= 3 weeks).

Arm title	Atezolizumab + Chemotherapy

Arm description:

Participants received atezolizumab, 1200 milligrams (mg), by IV infusion on Day 1 of each cycle along with either gemcitabine, 1000 mg/m^2, followed by carboplatin target AUC 2 mg/ml/min, both administered by IV infusion on Days 1 and 8 of each cycle or capecitabine, 1000 mg/m^2, BID, orally on Days 1 to 14, followed by a 7-day rest period in each cycle (1 Cycle = 3 weeks). Treatment was continued until PD, unacceptable toxicity, death or participant or investigator decision to discontinue treatment.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	RO5541267
Other name	MPDL3280A
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received atezolizumab 1200 mg, by IV infusion on Day 1 of each cycle (1 Cycle = 3 weeks)

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received gemcitabine, 1000 mg/m^2, administered by IV infusion on Days 1 and 8 of each cycle, followed by a 7-day rest period in each cycle (1 Cycle= 3 weeks).

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received capecitabine 1000 mg/m^2, BID, orally on Days 1 to 14, followed by a 7-day rest period in each cycle (1 Cycle= 3 weeks).

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received carboplatin target AUC 2 mg/ml/min, administered by IV infusion on Days 1 and 8 of each cycle, followed by a 7-day rest period in each cycle (1 Cycle= 3 weeks).

Number of subjects in period 1	Placebo + Chemotherapy	Atezolizumab + Chemotherapy
Started	298	297
Safety-evaluable Population	294	293
PD-L1-positive Population	177	177
mITT Population	192	188
Completed	0	0
Not completed	298	297
Consent withdrawn by subject	20	25

Physician decision	-	1
Study Ended by Sponsor	37	38
Protocol Deviation	-	1
Death	228	215
Lost to follow-up	13	16
Reason not Specified	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo + Chemotherapy
Reporting group description:	
Participants received atezolizumab matching placebo, by intravenous (IV) infusion on Day 1 of each cycle along with either gemcitabine, 1000 milligrams per square meter (mg/m^2), followed by carboplatin target under the curve (AUC) 2 milligrams per milliliter per minute (mg/ml/min), both administered by IV infusion on Days 1 and 8 of each cycle or capecitabine 1000 mg/m^2 , twice daily (BID), orally on Days 1 to 14, followed by a 7-day rest period in each cycle (1 Cycle= 3 weeks). Treatment was continued until disease progression (PD), unacceptable toxicity, death or participant or investigator decision to discontinue treatment.	
Reporting group title	Atezolizumab + Chemotherapy
Reporting group description:	
Participants received atezolizumab, 1200 milligrams (mg), by IV infusion on Day 1 of each cycle along with either gemcitabine, 1000 mg/m^2, followed by carboplatin target AUC 2 mg/ml/min, both administered by IV infusion on Days 1 and 8 of each cycle or capecitabine, 1000 mg/m^2, BID, orally on Days 1 to 14, followed by a 7-day rest period in each cycle (1 Cycle = 3 weeks). Treatment was continued until PD, unacceptable toxicity, death or participant or investigator decision to discontinue treatment.	

Reporting group values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy	Total
Number of subjects	298	297	595
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	49.4	48.6	
standard deviation	± 11.7	± 10.9	-
Sex: Female, Male			
Units: participants			
Female	298	297	595
Male	0	0	0
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	3	5	8
Asian	66	69	135
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	10	9	19
White	199	184	383
More than one race	0	2	2
Unknown or Not Reported	20	28	48
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	59	51	110
Not Hispanic or Latino	222	218	440
Unknown or Not Reported	17	28	45

End points

End points reporting groups

Reporting group title	Placebo + Chemotherapy

Reporting group description:

Participants received atezolizumab matching placebo, by intravenous (IV) infusion on Day 1 of each cycle along with either gemcitabine, 1000 milligrams per square meter (mg/m^2), followed by carboplatin target under the curve (AUC) 2 milligrams per milliliter per minute (mg/ml/min), both administered by IV infusion on Days 1 and 8 of each cycle or capecitabine 1000 mg/m^2 , twice daily (BID), orally on Days 1 to 14, followed by a 7-day rest period in each cycle (1 Cycle= 3 weeks). Treatment was continued until disease progression (PD), unacceptable toxicity, death or participant or investigator decision to discontinue treatment.

Reporting group title	Atezolizumab + Chemotherapy

Reporting group description:

Participants received atezolizumab, 1200 milligrams (mg), by IV infusion on Day 1 of each cycle along with either gemcitabine, 1000 mg/m^2, followed by carboplatin target AUC 2 mg/ml/min, both administered by IV infusion on Days 1 and 8 of each cycle or capecitabine, 1000 mg/m^2, BID, orally on Days 1 to 14, followed by a 7-day rest period in each cycle (1 Cycle = 3 weeks). Treatment was continued until PD, unacceptable toxicity, death or participant or investigator decision to discontinue treatment.

Primary: Overall Survival (OS) in Programmed Death Ligand 1 (PD-L1)-positive Population

End point title	Overall Survival (OS) in Programmed Death Ligand 1 (PD-L1)-positive Population

End point description:

OS was defined as time from randomization to death from any cause. Participants without a reported death event at the time of the analysis were censored on the date they were last known to be alive. If no post-baseline data were available, OS was censored at the date of randomization +1 day. PD-L1 positive population included all participants randomized in the study whose PD-L1 status was tumor-infiltrating immune cells (IC) of 1% or greater (IC1/2/3) at the time of randomization, grouped according to their assigned treatment arm, whether or not the assigned study treatment was received.

End point type	Primary

End point timeframe:

Time from randomization to death (Up to 68 months)

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	177		
Units: months				
median (confidence interval 95%)	11.24 (9.00 to 13.31)	12.09 (10.12 to 15.08)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy

Number of subjects included in analysis	354
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5891
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.2

Primary: OS in Modified Intent-to-treat (mITT) Population

End point title	OS in Modified Intent-to-treat (mITT) Population

End point description:

OS was defined as time from randomization to death from any cause. Participants without a reported death event at the time of the analysis were censored on the date they were last known to be alive. If no post-baseline data were available, OS was censored at the date of randomization +1 day. mITT population included all participants randomized under the protocol versions prior to version 4.0 (referred to as all-comers, i.e., PD-L1(SP142)-positive and PD-L1(SP142)-negative participants), grouped according to their assigned treatment arm, whether or not the assigned study treatment was received.

End point type	Primary

End point timeframe:

Time from randomization to death (Up to 68 months)

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	188		
Units: months				
median (confidence interval 95%)	9.79 (8.44 to 11.96)	10.35 (8.90 to 12.88)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6139
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.94

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.18

Secondary: 12-month Survival Rate in PD-L1-positive Population

End point title	12-month Survival Rate in PD-L1-positive Population

End point description:

12-month survival rate was defined as the percentage of participants alive 12 months after randomization. The 12-month survival rates were estimated by Kaplan-Meier methodology. PD-L1 positive population included all participants randomized in the study whose PD-L1 status was tumor-infiltrating IC of 1% or greater (IC1/2/3) at the time of randomization, grouped according to their assigned treatment arm, whether or not the assigned study treatment was received. Percentages have been rounded off to the nearest whole number.

End point type	Secondary

End point timeframe:

12 months

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	177		
Units: percentage of participants				
number (confidence interval 95%)	47.58 (39.92 to 55.23)	50.26 (42.61 to 57.91)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	354
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6264
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	2.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.14
upper limit	13.51

Secondary: 12-month Survival Rate in mITT Population

End point title	12-month Survival Rate in mITT Population

End point description:

12-month survival rate was defined as the percentage of participants alive 12 months after randomization. The 12-month survival rates were estimated by Kaplan-Meier methodology. mITT population included all participants randomized under the protocol versions prior to version 4.0 (referred to as all-comers, i.e., PD-L1(SP142)-positive and PD-L1(SP142)-negative participants), grouped according to their assigned treatment arm, whether or not the assigned study treatment was received. Percentages have been rounded off to the nearest whole number.

End point type	Secondary

End point timeframe:

12 months

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	188		
Units: percentage of participants				
number (confidence interval 95%)	42.44 (35.23 to 49.66)	46.20 (38.84 to 53.56)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.475
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	3.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.55
upper limit	14.07

Secondary: 18-month Survival Rate in PD-L1-positive Population

End point title	18-month Survival Rate in PD-L1-positive Population

End point description:

18-month survival rate was defined as the percentage of participants alive 18 months after randomization. The 18-month survival rates were estimated by Kaplan-Meier methodology. PD-L1 positive population included all participants randomized in the study whose PD-L1 status was tumor-infiltrating IC of 1% or greater (IC1/2/3) at the time of randomization, grouped according to their assigned treatment arm, whether or not the assigned study treatment was received. Percentages have been rounded off to the nearest whole number.

End point type	Secondary
End point timeframe:	
18 months	

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	177		
Units: percentage of participants				
number (confidence interval 95%)	32.48 (25.07 to 39.89)	33.63 (26.05 to 41.21)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	354
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8315
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.45
upper limit	11.75

Secondary: 18-month Survival Rate in mITT Population

End point title	18-month Survival Rate in mITT Population
End point description:	
18-month survival rate was defined as the percentage of participants alive 18 months after randomization. The 18-month survival rates were estimated by Kaplan-Meier methodology. mITT population included all participants randomized under the protocol versions prior to version 4.0 (referred to as all-comers, i.e., PD-L1(SP142)-positive and PD-L1(SP142)-negative participants), grouped according to their assigned treatment arm, whether or not the assigned study treatment was received. Percentages have been rounded off to the nearest whole number.	
End point type	Secondary
End point timeframe:	
18 months	

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	188		
Units: percentage of participants				
number (confidence interval 95%)	25.68 (19.15 to 32.21)	27.05 (20.39 to 33.71)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7738
Method	Z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.96
upper limit	10.69

Secondary: Progression-Free Survival (PFS) in PD-L1-positive Population

End point title	Progression-Free Survival (PFS) in PD-L1-positive Population

End point description:

PFS time from randomization to the first occurrence of PD, as determined by the investigator according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1), or death from any cause, whichever occurs first. PD = as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum of diameters at prior timepoints (including baseline). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of ≥5 millimeters (mm). Data for participants not experiencing PD/death were censored at the last tumour assessment date. If no tumor assessment was performed after randomisation, data were censored at date of randomisation +1 day. PD-L1 positive population = all participants randomized in the study whose PD-L1 status was tumor-infiltrating IC of 1% or greater (IC1/2/3) at the time of randomization, grouped according to their assigned treatment arm, whether or not assigned study treatment was received.

End point type	Secondary

End point timeframe:

Time from randomization to the first occurrence of PD or death (Up to 68 months)

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	177		
Units: months				
median (confidence interval 95%)	3.58 (3.35 to 4.17)	4.21 (3.71 to 5.62)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	354
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1387
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.06

Secondary: Objective Response Rate (ORR) in Response-evaluable Population, Subset of PD-L1-positive Population

End point title	Objective Response Rate (ORR) in Response-evaluable Population, Subset of PD-L1-positive Population

End point description:

ORR was defined as percentage of participants with measurable disease at baseline who achieved a documented unconfirmed objective response (OR). OR = either a complete response (CR) or a partial response (PR), as determined by the investigator according to RECIST v1.1. CR = disappearance of all target lesions. Any pathological lymph nodes must have a reduction in short axis to <10 millimeters (mm). PR = at least a 30% decrease in the sum of diameters (SOD) of target lesions, taking as reference the baseline SOD, in the absence of CR. PD-L1 positive population included all participants randomized in the study whose PD-L1 status was tumor-infiltrating IC of 1% or greater (IC1/2/3) at the time of randomization, grouped according to their assigned treatment arm, whether or not the assigned study treatment was received. Response-evaluable population included participants randomized in the study with measurable disease at baseline. Percentages have been rounded off to nearest whole number.

End point type	Secondary

End point timeframe:

Baseline up to end of study (Up to 68 months)

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	154		
Units: percentage of participants				
number (confidence interval 95%)	28.3 (21.45 to 35.98)	39.6 (31.83 to 47.80)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0337
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in ORR
Point estimate	11.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	22.37

Secondary: PFS in mITT Population

End point title	PFS in mITT Population

End point description:

PFS was defined as the time from randomization to the first occurrence of PD, as determined by the investigator according to RECIST v1.1, or death from any cause, whichever occurs first. PD was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum of diameters at prior timepoints (including baseline). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of ≥5 mm. Data for participants not experiencing PD or death were censored at the last tumour assessment date. If no tumor assessment was performed after randomisation, data were censored at the date of randomisation +1 day. mITT population included all participants randomized under the protocol versions prior to version 4.0 (referred to as all-comers, i.e., PD-L1(SP142)-positive and PD-L1(SP142)-negative participants), grouped according to their assigned treatment arm, whether or not the assigned study treatment was received.

End point type	Secondary

End point timeframe:

Time from randomization to the first occurrence of PD or death (Up to 68 months)

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	188		
Units: months				
median (confidence interval 95%)	3.58 (3.06 to 3.81)	3.71 (2.83 to 4.01)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7317
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.19

Secondary: ORR in Response-evaluable Population, Subset of mITT Population

End point title	ORR in Response-evaluable Population, Subset of mITT Population

End point description:

ORR was defined as percentage of participants with measurable disease at baseline who achieved a documented unconfirmed OR. OR was defined as either a CR or PR, as determined by the investigator according to RECIST v1.1. CR was defined as the disappearance of all target lesions. Any pathological lymph nodes must have a reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the SOD of target lesions, taking as reference the baseline SOD, in the absence of CR. mITT population included all participants randomized under the protocol versions prior to version 4.0 (referred to as all-comers, i.e., PD-L1(SP142)-positive and PD-L1(SP142)-negative participants), grouped according to their assigned treatment arm, whether or not the assigned study treatment was received. Response-evaluable Population included participants randomized in the study with measurable disease at baseline. Percentages have been rounded off to nearest whole number.

End point type	Secondary

End point timeframe:

Baseline up to end of study (Up to 68 months)

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	171		
Units: percentage of participants				
number (confidence interval 95%)	32.1 (25.16 to 39.77)	31.0 (24.16 to 38.51)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	339
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9755
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in ORR
Point estimate	-1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.63
upper limit	9.34

Secondary: Duration of Objective Response (DoR) in DoR-evaluable Population Subset of PD-L1-positive Population

End point title	Duration of Objective Response (DoR) in DoR-evaluable Population Subset of PD-L1-positive Population

End point description:

DoR=time from first occurrence of a documented unconfirmed response (CR/PR) until the date of PD per investigator using RECIST v1.1 or death from any cause, whichever occurs first. CR=disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to <10 mm. PR= ≥30% decrease in SOD of target lesions, taking as reference baseline SOD, in absence of CR. PD= ≥20% increase in SOD of target lesions, taking as reference smallest sum on study, including baseline, in addition to relative increase of 20%, sum must also demonstrate absolute increase of ≥5 mm. Appearance of one or more new lesions was also considered progression. PD-L1 positive population=all participants randomized in study whose PD-L1 status was tumor-infiltrating IC of 1% or greater (IC1/2/3) at time of randomization, grouped as per assigned arm, whether assigned treatment was received. DOR-evaluable population=participants randomized in study with measurable disease at baseline & OR.

End point type	Secondary

End point timeframe:

Time from the first occurrence of a documented OR until the date of PD/death (Up to 68 months)

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	61		
Units: months				
median (confidence interval 95%)	4.14 (3.45 to 5.78)	6.60 (4.63 to 8.02)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	106
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1359
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.11

Secondary: DoR in DoR-evaluable Population Subset of mITT Population

End point title	DoR in DoR-evaluable Population Subset of mITT Population

End point description:

DoR= time from first occurrence of a documented unconfirmed response (CR/PR) until date of PD per investigator using RECIST v1.1 or death from any cause, whichever occurs first. CR=disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to <10 mm. PR= ≥30% decrease in SOD of target lesions, taking as reference baseline SOD, in absence of CR. PD= ≥20% increase in SOD of target lesions, taking as reference smallest sum on study, including baseline, in addition to relative increase of 20%, sum must also demonstrate absolute increase of ≥5 mm. Appearance of one or more new lesions was considered progression. mITT population=all participants randomized under protocol versions prior to version 4.0 (referred to as all-comers, i.e., PD-L1(SP142)-positive & PD-L1(SP142)-negative), grouped as per assigned arm, whether assigned treatment was received. DOR-evaluable population=participants randomized in study with measurable disease at baseline & OR.

End point type	Secondary

End point timeframe:

Time from the first occurrence of a documented OR until the date of PD/death (Up to 68 months)

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	54	53		
Units: months				
median (confidence interval 95%)	5.22 (3.81 to 6.60)	5.70 (4.17 to 7.92)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	107
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8225
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.43

Secondary: Clinical Benefit Rate (CBR) in Response-evaluable Population Subset of PD-L1-positive Population

End point title	Clinical Benefit Rate (CBR) in Response-evaluable Population Subset of PD-L1-positive Population

End point description:

CBR=percentage of participants with either an unconfirmed CR/PR /stable disease (SD) that lasts at least 6 months per investigator according to RECIST v1.1. CR=disappearance of all target lesions. Any pathological lymph nodes must have a reduction in short axis to <10 mm. PR= ≥30% decrease in SOD of target lesions, taking as reference baseline SOD, in absence of CR. SD=neither sufficient shrinkage to qualify for CR or PR nor sufficient increase to qualify for PD. PD= ≥20% increase in SOD of target lesions, taking as reference the smallest SOD at prior timepoints (including baseline). In addition to relative increase of 20%, sum must also demonstrate an absolute increase of ≥5 mm. PD-L1 positive population=all participants randomized in study whose PD-L1 status was tumor-infiltrating IC of 1% or greater (IC1/2/3) at time of randomization, grouped according to their assigned treatment arm, whether or not the assigned study treatment was received. Response-evaluable population.

End point type	Secondary

End point timeframe:

Up to 68 months

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	154		
Units: percentage of participants				
number (confidence interval 95%)	34.6 (27.23 to 42.53)	42.9 (34.92 to 51.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: Confirmed Objective Response Rate (C-ORR) in Response-evaluable Population Subset of PD-L1-positive Population

End point title	Confirmed Objective Response Rate (C-ORR) in Response-evaluable Population Subset of PD-L1-positive Population

End point description:

C-ORR was defined as percentage of participants with measurable disease at baseline who achieved a documented confirmed OR. OR was defined as either a CR or PR, as determined by the investigator according to RECIST v1.1. CR was defined as the disappearance of all target lesions. Any pathological lymph nodes must have a reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the SOD of target lesions, taking as reference the baseline SOD, in the absence of CR. PD-L1 positive population included all participants randomized in the study whose PD-L1 status was tumor-infiltrating IC of 1% or greater (IC1/2/3) at the time of randomization, grouped according to their assigned treatment arm, whether or not the assigned study treatment was received. Response-evaluable population included participants randomized in the study with measurable disease at baseline. Percentages have been rounded off to nearest whole number.

End point type	Secondary

End point timeframe:

Up to 68 months

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	159	154		
Units: percentage of participants				
number (confidence interval 95%)	19.5 (13.65 to 26.52)	31.2 (23.96 to 39.12)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy

Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0172
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in ORR
Point estimate	11.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.47
upper limit	21.87

Secondary: CBR in Response-evaluable Population Subset of mITT Population

End point title	CBR in Response-evaluable Population Subset of mITT Population

End point description:

CBR=percentage of participants with either an unconfirmed CR/PR/SD that lasts at least 6 months per investigator according to RECIST v1.1. CR=disappearance of all target lesions. Any pathological lymph nodes must have a reduction in short axis to <10 mm. PR= ≥30% decrease in SOD of target lesions, taking as reference baseline SOD, in absence of CR. SD=neither sufficient shrinkage to qualify for CR or PR nor sufficient increase to qualify for PD. PD= ≥20% increase in SOD of target lesions, taking as reference the smallest SOD at prior timepoints (including baseline). In addition to relative increase of 20%, sum must also demonstrate an absolute increase of ≥5 mm. mITT population=all participants randomized under protocol versions prior to version 4.0 (referred to as all-comers, i.e., PD-L1(SP142)-positive & PD-L1(SP142)-negative participants, grouped according to their assigned arm, whether or not the assigned study treatment was received. Response-evaluable population.

End point type	Secondary

End point timeframe:

Up to 68 months

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	171		
Units: percentage of participants				
number (confidence interval 95%)	36.3 (29.04 to 44.07)	35.1 (27.96 to 42.74)		

Statistical analyses

No statistical analyses for this end point

Secondary: C-ORR in Response-evaluable Population Subset of mITT Population

End point title	C-ORR in Response-evaluable Population Subset of mITT Population

End point description:

C-ORR was defined as percentage of participants with measurable disease at baseline who achieved a documented confirmed OR. OR was defined as either a CR or PR, as determined by the investigator according to RECIST v1.1. CR was defined as the disappearance of all target lesions. Any pathological lymph nodes must have a reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the SOD of target lesions, taking as reference the baseline SOD, in the absence of CR. mITT population included all participants randomized under the protocol versions prior to version 4.0 (referred to as all-comers, i.e., PD-L1(SP142)-positive and PD-L1(SP142)-negative participants), grouped according to their assigned treatment arm, whether or not the assigned study treatment was received. Response-evaluable population included participants randomized in the study with measurable disease at baseline. Percentages have been rounded off to nearest whole number.

End point type	Secondary

End point timeframe:

Up to 68 months

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	171		
Units: percentage of participants				
number (confidence interval 95%)	23.2 (17.06 to 30.34)	23.4 (17.27 to 30.46)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Statistical analysis description:	
Stratified Analysis	
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	339
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8679
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in ORR
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.41
upper limit	9.77

Secondary: DoR for Confirmed Responders (C-DoR) in C-DoR-evaluable Population Subset of PD-L1-positive Population

End point title	DoR for Confirmed Responders (C-DoR) in C-DoR-evaluable Population Subset of PD-L1-positive Population

End point description:

C-DoR = time from the first occurrence of a documented confirmed response (CR /PR) until date of PD per investigator from tumor assessments using RECIST v1.1 or death from any cause, whichever occurs first. CR = disappearance of all target lesions. Any pathological lymph nodes must have a reduction in short axis to <10 mm. PR = ≥30% decrease in the SOD of target lesions, taking as reference the baseline SOD, in absence of CR. PD = ≥20% increase in SOD of target lesions, taking as reference smallest sum on study, including baseline, in addition to relative increase of 20%, sum must also demonstrate an absolute increase of at least 5 mm. Appearance of one or more new lesions was also considered progression. PD-L1 population = all participants randomized in study whose PD-L1 status was tumor-infiltrating IC of 1% or greater (IC1/2/3) at time of randomization, grouped according to their assigned treatment arm, whether assigned study treatment was received. C-DOR-evaluable population.

End point type	Secondary

End point timeframe:

Time from the first occurrence of a documented OR until the date of PD/death (Up to 68 months)

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	48		
Units: months				
median (confidence interval 95%)	5.78 (4.21 to 8.48)	7.92 (6.60 to 12.78)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2846
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	1.26

Secondary: C-DoR in C-DoR-evaluable Population Subset of mITT Population

End point title	C-DoR in C-DoR-evaluable Population Subset of mITT Population

End point description:

C-DoR = time from first occurrence of a documented confirmed response (CR/PR) until date of PD per investigator from tumor assessments using RECIST v1.1 or death from any cause, whichever occurs first. CR = disappearance of all target lesions. Any pathological lymph nodes must have a reduction in

short axis to <10 mm. PR = ≥30% decrease in SOD of target lesions, taking as reference baseline SOD, in absence of CR. PD = ≥20% increase in SOD of target lesions, taking as reference smallest sum on study, including baseline, in addition to relative increase of 20%, sum must also demonstrate an absolute increase of at least 5 mm. Appearance of one or more new lesions was also considered progression. mITT population = all participants randomized under protocol versions prior to version 4.0 (referred to as all-comers, i.e., PD-L1(SP142)-positive & PD-L1(SP142)-negative participants, grouped per assigned treatment arm, whether assigned study treatment was received. C-DOR-evaluable population.

End point type	Secondary

End point timeframe:

Time from the first occurrence of a documented OR until the date of PD/death (Up to 68 months)

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	40		
Units: months				
median (confidence interval 95%)	6.51 (4.83 to 8.48)	7.43 (5.55 to 12.98)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9853
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.61

Secondary: Time to Confirmed Deterioration (TTD) in Global Health Status/Quality of Life (GHS/QoL) According to the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC QLQ-C30) in PD-L1-positive Population

End point title	Time to Confirmed Deterioration (TTD) in Global Health Status/Quality of Life (GHS/QoL) According to the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC QLQ-C30) in PD-L1-positive Population

End point description:

TTD in GHS/QoL=minimally important decrease of ≥10 points at 2 consecutive assessment time-points

on GHS/QoL scale (Items 29, 30) of EORTC QLQ-C30, consisting of 30 questions that assess 5 aspects of participant functioning (physical, emotional, role, cognitive & social), 3 symptom scales (fatigue, nausea & vomiting & pain), GHS & QoL & 6 single items (dyspnea, insomnia, appetite loss, constipation, diarrhea & financial difficulties) with a recall period of the previous week. Participant responses to questions regarding GHS (Question 29: "How would you rate your overall health during the past week?") & QoL (Question 30: "How would you rate your overall quality of life during the past week?") were assessed & were scored on a 7-point scale (1=Very poor; 7=Excellent). Scores are linearly transformed on a scale of 0-100. High score indicating better QoL. PD-L1 positive population. 999=upper limit of the 95% CI was not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

Up to 68 months

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	177		
Units: months				
median (confidence interval 95%)	6.77 (4.30 to 32.69)	9.43 (6.01 to 999)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy
Statistical analysis description:	
Stratified Analysis	
Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	354
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4117
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.21

Secondary: TTD in GHS/QoL According to EORTC QLQ-C30 in mITT Population

End point title	TTD in GHS/QoL According to EORTC QLQ-C30 in mITT Population

End point description:

TTD in GHS/QoL, minimally important decrease of ≥10 points at 2 consecutive assessment time-points on the GHS/QoL scale (Items 29, 30) of EORTC QLQ-C30, consisting of 30 questions that assess 5 aspects of participant functioning (physical, emotional, role, cognitive & social), 3 symptom scales (fatigue, nausea & vomiting & pain), GHS & QoL & 6 single items (dyspnea, insomnia, appetite loss,

constipation, diarrhea & financial difficulties) with a recall period of the previous week. Participant responses to questions (Q) on GHS (Q29: "How would you rate your overall health during the past week?") & QoL (Q30: "How would you rate your overall quality of life during the past week?") were assessed & were scored on a 7-point scale (1=Very poor; 7=Excellent). Scores were linearly transformed on 0-100 scale. High score= better QoL. mITT population=all participants randomized under protocol versions prior to v4.0 (all-comers, i.e., PD-L1(SP142)-positive & PD-L1(SP142)-negative participants.

End point type	Secondary

End point timeframe:

Up to 68 months

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	188		
Units: months				
median (confidence interval 95%)	7.66 (4.34 to 32.69)	8.90 (5.88 to 16.82)		

Statistical analyses

Statistical analysis title	Placebo+Chemotherapy vs Atezolizumab+Chemotherapy

Statistical analysis description:

Stratified Analysis

Comparison groups	Placebo + Chemotherapy v Atezolizumab + Chemotherapy
Number of subjects included in analysis	380
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7215
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.3

Secondary: Serum Concentration of Atezolizumab

End point title	Serum Concentration of Atezolizumab[1]

End point description:

Pharmacokinetic (PK)-evaluable population included participants who received any dose of study medication and who had at least one evaluable post-baseline PK sample. n= number of participants with data available for analyses at the specified timepoints. 9999= Geometric mean & geometric coefficient of variation were not estimable as samples were below the limit of quantification.

End point type	Secondary

End point timeframe:

Pre-dose on Day 1 of Cycles 1, 2, 3 and 4; Post-dose on Day 1 of Cycles 1 and 3 and Treatment Discontinuation Visit (up to 69 months) (1 Cycle= 3 weeks)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Serum concentration was assessed for atezolizumab only.

End point values	Atezolizumab + Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	268			
Units: micrograms/millilitre (µg/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 Predose (n=268)	9999 (± 9999)			
Cycle 1 Day 1 Post-dose (n=263)	442 (± 59.7)			
Cycle 2 Day 1 Pre-dose (n=262)	87.2 (± 72.7)			
Cycle 3 Day 1 Predose (n=223)	140 (± 42.9)			
Cycle 3 Day 1 Postdose (n=205)	517 (± 47.7)			
Cycle 4 Day 1 Predose (n=167)	157 (± 104.9)			
Treatment Discontinuation (n=187)	120 (± 189.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events (AEs)

End point title	Number of Participants With Adverse Events (AEs)

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product, regardless of causal attribution. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions that worsen during a study are also considered AEs. Safety-evaluable population included participants who received any amount of any study drug (atezolizumab/placebo or chemotherapy).

End point type	Secondary

End point timeframe:

From treatment initiation up to 90 days after last dose (up to 71 months)

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	293		
Units: participants	283	281		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-Drug Antibodies (ADAs) to Atezolizumab

End point title	Number of Participants With Anti-Drug Antibodies (ADAs) to Atezolizumab[2]

End point description:

Number of ADA-positive participants after drug administration was determined for participants exposed to atezolizumab. For determining post-baseline incidence, participants were considered to be ADA-positive if they were ADA-negative or had missing data at baseline but developed an ADA response following study drug exposure, or if they were ADA-positive at baseline and the titer of 1 or more post-baseline samples was at least 0.60 titer units (t.u.) greater than the baseline titer result. The sum of participants who were ADA-positive at postbaseline visits of Cycles 1 to 4 and treatment discontinuation has been reported here. Safety-evaluable population included participants who received any amount of any study drug (atezolizumab/placebo or chemotherapy). Number analyzed included participants with data available for analysis.

End point type	Secondary

End point timeframe:

Cycles 1 to 4 and Treatment Discontinuation visit (up to 69 months)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: ADA 's were assessed for atezolizumab only.

End point values	Atezolizumab + Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	275			
Units: participants	20			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With PD-L1 Protein Expression in Screening Tumour Tissue and Post-baseline Assessment

End point title	Number of Participants With PD-L1 Protein Expression in Screening Tumour Tissue and Post-baseline Assessment

End point description:

FAS population included all participants randomized in the study, grouped according to their assigned treatment arm, whether or not the assigned study treatment was received. n = number of participants with data available for analyses at the specified category. 9999 = No participants were analyzed for the category.

End point type	Secondary

End point timeframe:

Baseline up to 68 months

End point values	Placebo + Chemotherapy	Atezolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	298	297		
Units: participants				
Baseline IC0- Post-baseline IC0 (n=298,297)	3	0		
Baseline IC1/2/3- Post-baseline IC0 (n=298,297)	0	0		
Baseline IC0- Post-baseline IC1/2/3 (n=298,297)	0	0		
BaselineIC1/2/3- Post-baselineIC1/2/3 (n=298,297)	6	2		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: 12-month Survival Rate in China Population

End point title	12-month Survival Rate in China Population[3]

End point description:

12-month survival rate was defined as the percentage of participants alive 12 months after randomization. As pre-specified in the SAP, analysis for China population was to be conducted based on data maturity and estimated treatment effect from the global population. As the results for the global population did not meet pre-specified criteria, a separate analysis for China subpopulation was not conducted.

End point type	Other pre-specified

End point timeframe:

12 months

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for China population only.

End point values	Placebo + Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	0[4]			
Units: percentage of participants				
number (confidence interval 95%)	(to)			

Notes:

[4] - No separate analysis was performed for the China population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: 18-month Survival Rate in China Population

End point title	18-month Survival Rate in China Population[5]

End point description:

18-month survival rate was defined as the percentage of participants alive 18 months after randomization. As pre-specified in the SAP, analysis for China population was to be conducted based on data maturity and estimated treatment effect from the global population. As the results for the global

population did not meet pre-specified criteria, a separate analysis for China subpopulation was not conducted.

End point type	Other pre-specified

End point timeframe:

18 months

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for China population only.

End point values	Placebo + Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: percentage of participants				
number (confidence interval 95%)	(to)			

Notes:

[6] - No separate analysis was performed for the China population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: PFS in China Population

End point title	PFS in China Population[7]

End point description:

PFS was defined as the time from randomization to the first occurrence of PD, as determined by the investigator according to RECIST 1.1, or death from any cause, whichever occurs first. As pre-specified in the SAP, analysis for China population was to be conducted based on data maturity and estimated treatment effect from the global population. As the results for the global population did not meet pre-specified criteria, a separate analysis for China subpopulation was not conducted.

End point type	Other pre-specified

End point timeframe:

Time from randomization to the first occurrence of PD or death (Up to 68 months)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for China population only.

End point values	Placebo + Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	0[8]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[8] - No separate China analysis was done.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: OS in China Population

End point title	OS in China Population[9]

End point description:

OS was defined as time from randomization to death from any cause. As pre-specfied in the SAP, analysis for China population was to be conducted based on data maturity and estimated treatment effect from the global population. As pre-specified in the SAP, analysis for China population was to be conducted based on data maturity and estimated treatment effect from the global population. As the results for the global population did not meet pre-specified criteria, a separate analysis for China subpopulation was not conducted.

End point type	Other pre-specified

End point timeframe:

Time from randomization to death (Up to 68 months)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for China population only.

End point values	Placebo + Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	0[10]			
Units: percentage of participants				
median (confidence interval 95%)	(to)			

Notes:

[10] - No separate analysis was performed for the China population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: ORR in China Population

End point title	ORR in China Population[11]

End point description:

ORR= percentage of participants with measurable disease at baseline who achieved a documented unconfirmed OR. OR= either a CR or PR, as determined by the investigator according to RECIST v1.1. CR= disappearance of all target lesions. Any pathological lymph nodes must have a reduction in short axis to <10 mm. PR= at least a 30% decrease in the SOD of target lesions, taking as reference the baseline SOD, in the absence of CR. As pre-specified in the SAP, analysis for China population was to be conducted based on data maturity and estimated treatment effect from the global population. As the results for the global population did not meet pre-specified criteria, a separate analysis for China subpopulation was not conducted.

End point type	Other pre-specified

End point timeframe:

Baseline up to end of study (Up to 68 months)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for China population only.

End point values	Placebo + Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: percentage of participants				
number (confidence interval 95%)	(to)			

Notes:

[12] - No separate analysis was performed for the China population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: DoR in China Population

End point title	DoR in China Population[13]

End point description:

DoR=time from first occurrence of a documented unconfirmed OR (CR/PR) until date of PD per the investigator from tumor assessments using RECIST v1.1 or death from any cause, whichever occurs first. CR=disappearance of all target lesions. Any pathological lymph nodes must have a reduction in short axis to <10 mm. PR= ≥30% decrease in the SOD of target lesions, taking as reference baseline SOD, in absence of CR. PD= ≥20% increase in SOD of target lesions, taking as reference smallest sum on study, including baseline, in addition to relative increase of 20%, sum must also demonstrate an absolute increase of at least 5 mm. Appearance of one/more new lesions was also considered progression. As pre-specified in SAP, analysis for China population was to be conducted based on data maturity and estimated treatment effect from the global population. As the results for the global population did not meet pre-specified criteria, separate analysis for China subpopulation was not conducted.

End point type	Other pre-specified

End point timeframe:

Time from the first occurrence of a documented OR until the date of PD/death (Up to 68 months)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for China population only.

End point values	Placebo + Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	0[14]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[14] - No separate analysis was performed for the China population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: C-ORR in China Population

End point title	C-ORR in China Population[15]

End point description:

C-ORR was defined as percentage of participants with measurable disease at baseline who achieved a documented confirmed OR. OR was defined as either a CR or PR, as determined by the investigator according to RECIST v1.1. CR was defined as the disappearance of all target lesions. Any pathological lymph nodes must have a reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the SOD of target lesions, taking as reference the baseline SOD, in the absence of CR. As pre-specified in the SAP, analysis for China population was to be conducted based on data maturity and estimated treatment effect from the global population. As the results for the global population did not

meet pre-specified criteria, a separate analysis for China subpopulation was not conducted.

End point type	Other pre-specified

End point timeframe:

Up to 68 months

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for China population only.

End point values	Placebo + Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	0[16]			
Units: percentage of participants				
number (confidence interval 95%)	(to)			

Notes:

[16] - No separate analysis was performed for the China population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: CBR in China Population

End point title	CBR in China Population[17]

End point description:

CBR= percentage of participants with either an unconfirmed CR/PR/SD that lasts at least 6 months as per investigator according to RECIST v1.1. CR= disappearance of all target lesions. Any pathological lymph nodes must have a reduction in short axis to <10 mm. PR= ≥30% decrease in SOD of target lesions, taking as reference baseline SOD, in absence of CR. SD= neither sufficient shrinkage to qualify for CR or PR nor sufficient increase to qualify for PD. PD= ≥20% increase in SOD of target lesions, taking as reference the smallest SOD at prior timepoints (including baseline). In addition to relative increase of 20%, sum must also demonstrate an absolute increase of ≥5 mm. As pre-specified in the SAP, analysis for China population was to be conducted based on data maturity and estimated treatment effect from the global population. As the results for the global population did not meet pre-specified criteria, a separate analysis for China subpopulation was not conducted.

End point type	Other pre-specified

End point timeframe:

Up to 68 months

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for China population only.

End point values	Placebo + Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	0[18]			
Units: percentage of participants				
number (confidence interval 95%)	(to)			

Notes:

[18] - No separate analysis was performed for the China population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: C-DoR in China Population

End point title	C-DoR in China Population[19]

End point description:

C-DoR=time from first occurrence of a documented confirmed response (CR/PR) until date of PD per the investigator from tumor assessments using RECIST v1.1 or death from any cause, whichever occurs first. CR=disappearance of all target lesions. Any pathological lymph nodes must have a reduction in short axis to <10 mm. PR= ≥30% decrease in the SOD of target lesions, taking as reference baseline SOD, in absence of CR. PD= ≥20% increase in SOD of target lesions, taking as reference smallest sum on study, including baseline, in addition to relative increase of 20%, sum must also demonstrate an absolute increase of at least 5 mm. Appearance of one/more new lesions was also considered progression. As pre-specified in SAP, analysis for China population was to be conducted based on data maturity and estimated treatment effect from the global population. As the results for the global population did not meet pre-specified criteria, separate analysis for China subpopulation was not conducted.

End point type	Other pre-specified

End point timeframe:

Time from the first occurrence of a documented OR until the date of PD/death (Up to 68 months)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting data for China population only.

End point values	Placebo + Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	0[20]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[20] - No separate analysis was performed for the China population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: TTD in GHS/QoL According to EORTC QLQ-C30 in China Population

End point title	TTD in GHS/QoL According to EORTC QLQ-C30 in China Population[21]

End point description:

TTD in GHS/QoL= minimally important decrease of ≥10 points at 2 consecutive assessment time-points on GHS/QoL scale (Items 29, 30) of EORTC QLQ-C30 consists of 30 questions that assess 5 aspects of participant functioning (physical, emotional, role, cognitive, & social), 3 symptom scales (fatigue, nausea & vomiting, &pain),GHS &QoL, & 6 single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, & financial difficulties) with a recall period of the previous week. Participant responses to questions regarding GHS (Question 29: "How would you rate your overall health during the past week?") & QoL (Question 30: "How would you rate your overall quality of life during the past week?") were assessed & were scored on a 7-point scale (1=Very poor;7=Excellent). Scores were transformed on scale of 0-100. High score= better QoL. As results for global population did not meet pre-specified criteria, separate analysis for China subpopulation was not conducted.

End point type	Other pre-specified

End point timeframe:

Up to 68 months

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is reporting data for China population only.

End point values	Placebo + Chemotherapy			
Subject group type	Reporting group			
Number of subjects analysed	0[22]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[22] - No separate analysis was performed for the China population.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From treatment initiation up to 90 days after last dose (up to 71 months)	
Adverse event reporting additional description:	
Safety-evaluable population included participants who received any amount of any study drug (atezolizumab/placebo or chemotherapy).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups	
Reporting group title	Atezolizumab + Chemotherapy
Reporting group description:	
Participants received atezolizumab 1200 mg, by IV infusion on Day 1 of each cycle along with either gemcitabine, 1000 mg/m^2, followed by carboplatin target AUC 2 mg/ml/min, both administered by IV infusion on Days 1 and 8 of each cycle or capecitabine, 1000 mg/m^2, BID, orally on Days 1 to 14, followed by a 7-day rest period in each cycle (1 Cycle = 3 weeks). Treatment was continued until PD, unacceptable toxicity, death or participant or investigator decision to discontinue treatment.	
Reporting group title	Placebo + Chemotherapy
Reporting group description:	
Participants received atezolizumab matching placebo, by IV infusion on Day 1 of each cycle along with either gemcitabine, 1000 mg/m^2, followed by carboplatin target AUC 2 mg/ml/min, both administered by IV infusion on Days 1 and 8 of each cycle or capecitabine, 1000 mg/m^2, BID, orally on Days 1 to 14, followed by a 7-day rest period in each cycle (1 Cycle= 3 weeks). Treatment was continued until PD, unacceptable toxicity, death or participant or investigator decision to discontinue treatment.	

Serious adverse events	Atezolizumab + Chemotherapy	Placebo + Chemotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	69 / 293 (23.55%)	57 / 294 (19.39%)	
number of deaths (all causes)	226	233	
number of deaths resulting from adverse events	5	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected neoplasm			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour associated fever			

subjects affected / exposed	2 / 293 (0.68%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Jugular vein thrombosis			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Axillary vein thrombosis			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (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	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 293 (1.02%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 293 (0.34%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonitis			
subjects affected / exposed	2 / 293 (0.68%)	3 / 294 (1.02%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pleural effusion			
subjects affected / exposed	4 / 293 (1.37%)	2 / 294 (0.68%)	
occurrences causally related to treatment / all	1 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune-mediated lung disease			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	3 / 293 (1.02%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	2 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pulmonary embolism			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 293 (0.00%)	2 / 294 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (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 Extrusion			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
White blood cell count decreased			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	7 / 293 (2.39%)	7 / 294 (2.38%)	
occurrences causally related to treatment / all	11 / 11	9 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	2 / 293 (0.68%)	2 / 294 (0.68%)	
occurrences causally related to treatment / all	3 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 293 (0.68%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Vascular access site pain			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			

subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation necrosis			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Poisoning			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Torsade de pointes			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Diabetic hyperglycaemic coma			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			

subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (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	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Syncope			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
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	3 / 293 (1.02%)	4 / 294 (1.36%)	
occurrences causally related to treatment / all	2 / 3	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood disorder			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	6 / 293 (2.05%)	8 / 294 (2.72%)	
occurrences causally related to treatment / all	6 / 6	10 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 293 (0.00%)	2 / 294 (0.68%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			

subjects affected / exposed	3 / 293 (1.02%)	2 / 294 (0.68%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelosuppression			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 293 (0.34%)	3 / 294 (1.02%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	2 / 293 (0.68%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 293 (0.34%)	3 / 294 (1.02%)	
occurrences causally related to treatment / all	1 / 1	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cytolysis			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Device related infection			

subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	4 / 293 (1.37%)	2 / 294 (0.68%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cellulitis			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acinetobacter bacteraemia			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (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	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 293 (0.00%)	3 / 294 (1.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 293 (0.68%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Influenza			
subjects affected / exposed	1 / 293 (0.34%)	0 / 294 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 293 (1.37%)	2 / 294 (0.68%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus infection			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastitis bacterial			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastitis			
subjects affected / exposed	1 / 293 (0.34%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangitis			

subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 293 (0.00%)	1 / 294 (0.34%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Atezolizumab + Chemotherapy	Placebo + Chemotherapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	276 / 293 (94.20%)	278 / 294 (94.56%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	95 / 293 (32.42%)	100 / 294 (34.01%)	
occurrences (all)	160	187	
White blood cell count decreased			
subjects affected / exposed	58 / 293 (19.80%)	64 / 294 (21.77%)	
occurrences (all)	227	178	
Platelet count decreased			

subjects affected / exposed	69 / 293 (23.55%)	69 / 294 (23.47%)	
occurrences (all)	169	171	
Neutrophil count decreased			
subjects affected / exposed	77 / 293 (26.28%)	88 / 294 (29.93%)	
occurrences (all)	311	249	
Lymphocyte count decreased			
subjects affected / exposed	23 / 293 (7.85%)	36 / 294 (12.24%)	
occurrences (all)	44	60	
Blood alkaline phosphatase increased			
subjects affected / exposed	19 / 293 (6.48%)	19 / 294 (6.46%)	
occurrences (all)	22	26	
Aspartate aminotransferase increased			
subjects affected / exposed	86 / 293 (29.35%)	91 / 294 (30.95%)	
occurrences (all)	138	195	
Nervous system disorders			
Dizziness			
subjects affected / exposed	23 / 293 (7.85%)	17 / 294 (5.78%)	
occurrences (all)	25	18	
Headache			
subjects affected / exposed	52 / 293 (17.75%)	54 / 294 (18.37%)	
occurrences (all)	70	73	
Blood and lymphatic system disorders			
Lymphopenia			
subjects affected / exposed	26 / 293 (8.87%)	17 / 294 (5.78%)	
occurrences (all)	40	34	
Leukopenia			
subjects affected / exposed	52 / 293 (17.75%)	42 / 294 (14.29%)	
occurrences (all)	153	130	
Anaemia			
subjects affected / exposed	133 / 293 (45.39%)	138 / 294 (46.94%)	
occurrences (all)	199	210	
Neutropenia			
subjects affected / exposed	108 / 293 (36.86%)	119 / 294 (40.48%)	
occurrences (all)	341	322	
Thrombocytopenia			

subjects affected / exposed	52 / 293 (17.75%)	54 / 294 (18.37%)	
occurrences (all)	117	123	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	49 / 293 (16.72%)	39 / 294 (13.27%)	
occurrences (all)	68	61	
Oedema peripheral			
subjects affected / exposed	17 / 293 (5.80%)	13 / 294 (4.42%)	
occurrences (all)	22	14	
Mucosal inflammation			
subjects affected / exposed	16 / 293 (5.46%)	14 / 294 (4.76%)	
occurrences (all)	18	19	
Fatigue			
subjects affected / exposed	69 / 293 (23.55%)	62 / 294 (21.09%)	
occurrences (all)	85	75	
Asthenia			
subjects affected / exposed	66 / 293 (22.53%)	73 / 294 (24.83%)	
occurrences (all)	95	93	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	17 / 293 (5.80%)	19 / 294 (6.46%)	
occurrences (all)	19	24	
Abdominal pain			
subjects affected / exposed	14 / 293 (4.78%)	18 / 294 (6.12%)	
occurrences (all)	16	23	
Vomiting			
subjects affected / exposed	67 / 293 (22.87%)	69 / 294 (23.47%)	
occurrences (all)	109	90	
Nausea			
subjects affected / exposed	121 / 293 (41.30%)	122 / 294 (41.50%)	
occurrences (all)	236	179	
Dyspepsia			
subjects affected / exposed	8 / 293 (2.73%)	16 / 294 (5.44%)	
occurrences (all)	8	19	
Diarrhoea			

subjects affected / exposed	46 / 293 (15.70%)	40 / 294 (13.61%)	
occurrences (all)	75	55	
Constipation			
subjects affected / exposed	61 / 293 (20.82%)	61 / 294 (20.75%)	
occurrences (all)	87	77	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	19 / 293 (6.48%)	23 / 294 (7.82%)	
occurrences (all)	21	25	
Cough			
subjects affected / exposed	38 / 293 (12.97%)	39 / 294 (13.27%)	
occurrences (all)	44	43	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	33 / 293 (11.26%)	22 / 294 (7.48%)	
occurrences (all)	49	25	
Pruritus			
subjects affected / exposed	24 / 293 (8.19%)	15 / 294 (5.10%)	
occurrences (all)	35	15	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	32 / 293 (10.92%)	29 / 294 (9.86%)	
occurrences (all)	40	34	
Alopecia			
subjects affected / exposed	21 / 293 (7.17%)	29 / 294 (9.86%)	
occurrences (all)	22	30	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	25 / 293 (8.53%)	19 / 294 (6.46%)	
occurrences (all)	26	21	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	25 / 293 (8.53%)	12 / 294 (4.08%)	
occurrences (all)	29	13	
Hyperthyroidism			
subjects affected / exposed	15 / 293 (5.12%)	0 / 294 (0.00%)	
occurrences (all)	17	0	

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	28 / 293 (9.56%)	30 / 294 (10.20%)	
occurrences (all)	30	35	
Bone pain			
subjects affected / exposed	10 / 293 (3.41%)	16 / 294 (5.44%)	
occurrences (all)	11	22	
Myalgia			
subjects affected / exposed	19 / 293 (6.48%)	19 / 294 (6.46%)	
occurrences (all)	25	20	
Pain in extremity			
subjects affected / exposed	24 / 293 (8.19%)	27 / 294 (9.18%)	
occurrences (all)	26	30	
Arthralgia			
subjects affected / exposed	40 / 293 (13.65%)	29 / 294 (9.86%)	
occurrences (all)	46	35	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	18 / 293 (6.14%)	13 / 294 (4.42%)	
occurrences (all)	26	20	
Urinary tract infection			
subjects affected / exposed	16 / 293 (5.46%)	9 / 294 (3.06%)	
occurrences (all)	22	9	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	50 / 293 (17.06%)	32 / 294 (10.88%)	
occurrences (all)	51	33	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 November 2017	Protocol v2: • Two exclusion criteria were added -Symptomatic or rapid visceral progression -No prior treatment with an anthracycline and taxane • Updates were made to the list of events requiring permanent discontinuation of atezolizumab/placebo (addition of any recurrent Grade 2 or 3 hypophysitis or Grade 4 hypophysitis) • A new appendix was added to the protocol, detailing the risks associated with atezolizumab, and providing guidelines for the management of AEs associated with atezolizumab.
18 February 2019	Protocol v3: • Inclusion criteria were updated • Safety updates were included based on the atezolizumab Investigator's Brochure (Version 14, dated October 2018) • Additional explanation was provided to clarify the conditions and process for unblinding in case of disease progression. • To correct a previous inconsistency within the protocol, references to measurements of capecitabine concentrations were removed. • Clarification was provided for cases where only one component of the study treatment (i.e., atezolizumab/placebo or chemotherapy) was discontinued permanently. In these cases, treatment with the other drugs may continue as long as the participants experienced clinical benefit. • Provisions had been included to allow the administration of carboplatin in exceptional cases of absolute neutrophil counts (ANC) being between >1500 and 1500 x 106 /L and platelet count ≥100,000 x 106 /L shows no evidence of fever or infection. • It was clarified that assessments on Day 8 of each cycle only applied to participants receiving carboplatin/gemcitabine, and that the coagulation panel tests on Day 1 of each cycle only applied to participants receiving capecitabine.

26 August 2019	Protocol v4: • Analysis of the primary endpoint was modified to occur hierarchically in the following fixed order: 1. OS in the PD-L1-positive population, 2. OS in the modified ITT population. • The primary analysis of OS to be completed when the required number of 247 mortality events have occurred in the PD-L1-positive subpopulation. • PFS and ORR were retained as secondary endpoints and were tested hierarchically after OS, in the PD-L1-positive population first, followed by the modified ITT population. • Two new secondary endpoints were added to the protocol: C-ORR and C-DoR. • To allow for the primary analysis of OS completed in the PD-L1-positive population, recruitment was to be extended as follows: after approximately 350 participants with inoperable recurrent TNBC had been randomised in the study, approximately 190 additional participants with PD-L1-positive tumour status were to be randomised. • The estimated total sample size was increased from 350 to 540 randomised participants. • The total study recruitment period was extended from 23 to 48 months. • It was anticipated that the final analysis of OS in the PD-L1-positive population would occur approximately 58 months (compared to the previously estimated 35 months in the modified ITT population) after FPI. • The analysis populations were updated as follows: -The PD-L1-positive subpopulation included all participants randomised in study whose tumour shows PD-L1 expression of ≥1%at the time of randomisation. -The modified ITT population included all participants randomised in study before protocol version 4.0. -Sensitivity analyses of OS were to be completed on the FAS population, defined as all participants randomised in the study (before and after protocol amendment 4.0). -Supplemental analyses of OS were to be conducted to assess the consistency of treatment effect in the PD-L1-positive population randomised before and after protocol version 4.0.
26 February 2020	Protocol v5: • New section was added to evaluate whether the efficacy of atezolizumab plus chemotherapy compared with placebo plus chemotherapy as measured by OS and other efficacy endpoints in the China population was consistent with the efficacy observed in the Global population. • Recruitment of all-comers was closed after 382 all-comers were randomised in the Global study (compared to the planned approximately 350 participants); of these, 140 (36.6%) had PD-L1-positive tumour status (compared to the previously estimated 40%). To enable the primary analysis of OS in 330 PD-L1- positive participants, approximately 190 additional participants with PD-L1-positive tumour status were to be randomised, for a total of 572 randomised participants in the Global study (compared to the previously planned 540 participants). • Additional participants with PD-L1-positive tumour status were subsequently randomised in to 1:1 ratio in China only, for a total enrolment of approximately 70 participants with PD-L1-positive tumour status in mainland China, referred to as the China population. • For participants randomised in China, the clinical cut-off (CCO) date for the final OS analysis was) when the target number of mortality events had occurred in the PD-L1-positive population. • Inclusion criterion #7 was updated to indicate that Chinese traditional medicines with an approved indication for cancer treatment were permitted as long as the last administration occurred at least 2 weeks prior to randomisation. • It was clarified that if additional enrolment in China was initiated, a separate analysis would be performed for the China population. • The final analysis of OS in the China population would be conducted when sufficient OS events had occurred. • The efficacy analyses would be unstratified for China Population instead of stratified.

21 December 2020	Protocol v6: • The list of approved indications for atezolizumab was updated to include unresectable or metastatic hepatocellular carcinoma and BRAF V600 mutation-positive unresectable or metastatic melanoma. • An updated summary of treatment-emergent (treatment-induced plus treatment-enhanced) anti-drug antibodies (ADAs) for Atezolizumab was included. • The anticipated length of recruitment was revised from 48 to 53 months. • The minimum survival follow-up has was updated from 10 to 5 months. • The requirement for the Sponsor and its agents, the investigator and research staff to remain blinded to PD-L1 status is no longer applicable, has been deleted. • It was clarified that completion of Patient-Reported Outcomes (PROs) after laboratory tests was permitted, provided there was no prior discussion of the participant's laboratory results or health record with clinic staff, and that the PROs were completed before drug administration. • The description of the EORTC QLQ-C30 scales and scoring was updated for better clarity. • General completion times were added for each PRO measure.
13 January 2021	Protocol v7: • The list of approved indications for atezolizumab was updated to include unresectable or metastatic hepatocellular carcinoma and BRAF V600 mutation-positive unresectable or metastatic melanoma. • Key updates include the insertion of the results for the: -Final overall survival (OS) analysis for Study WO29522 (IMpassion 130) -Primary analysis of progression-free survival (PFS) for Study MO39196 (IMpassion131)
12 November 2021	Protocol v8: • The list of approved indications for atezolizumab was updated. • The requirement for additional samples for ADA analyses from patients experiencing immune-mediated adverse events was removed • Clarification was added to indicate that herbal therapies not intended for the treatment of cancer may be used during the study at the discretion of the investigator. • Clarification was added that screening bone or PET scan must be performed to evaluate for bone metastases • Language regarding PFS events in participants with missing data will be relocated to the SAP
25 January 2023	Protocol v9: • Details on the timing of analysis of China population was provided to align with Statistical Analysis Plan (SAP) • The indication-specific companion diagnostics approval status of the VENTANA PD-L1 (SP142) Assay for the assessment of the PD-L1 protein was updated • Due to potentially still ongoing enrolment of participants in China at the time of primary endpoint analysis, clarification was added to indicate that treatment unblinding at the study level at the time of primary endpoint analysis only applied to randomized participants. Unblinding at the study level did not apply to participants who were not randomized at the time of primary endpoint analysis • PRO evaluable population was removed, as PRO analysis was done using PD-L1 (SP142) positive population and the mITT population

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported