EU Clinical Trials Register

Clinical trial results:
A Phase II, Randomized, Double-Blind Placebo-Controlled Study of Atezolizumab With or Without Bevacizumab in Combination With Cisplatin Plus Gemcitabine in Patients With Untreated, Advanced Biliary Tract Cancer

Summary

EudraCT number	2020-003759-14
Trial protocol	PL IT
Global end of trial date	

Results information

Result version number	v1
This version publication date	27 May 2023
First version publication date	27 May 2023

Trial information

Trial identification

Sponsor protocol code	GO42661

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04677504
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	16 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 May 2022
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the efficacy and safety of atezolizumab with bevacizumab in combination with cisplatin and gemcitabine (CisGem), compared with atezolizumab in combination with CisGem, in participants with advanced biliary tract cancer (BTC) (i.e., intrahepatic cholangiocarcinoma [iCCA], extrahepatic CCA [eCCA], or gallbladder cancer [GBC]) who did not received prior systemic therapy.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 February 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	China: 6
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Hong Kong: 2
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Korea, Republic of: 44
Country: Number of subjects enrolled	Poland: 11
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Thailand: 8
Country: Number of subjects enrolled	Turkey: 8
Country: Number of subjects enrolled	Taiwan: 9
Country: Number of subjects enrolled	Ukraine: 7
Country: Number of subjects enrolled	United States: 14
Worldwide total number of subjects	162
EEA total number of subjects	39

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)	89
From 65 to 84 years	73
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This is a global multicenter study.

Pre-assignment

Screening details:

This study included participants with advanced biliary tract cancer (i.e., intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, or gallbladder cancer) who did not receive prior systemic therapy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO

Arm description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received placebo matching bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

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

Dosage and administration details:

Atezolizumab was administered intravenously at a fixed dose of 1200 mg on Day 1 of each 21-day cycle.

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

Dosage and administration details:

Gemcitabine was administered intravenously at a dose of 1000 mg/m^2 on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

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

Dosage and administration details:

Cisplatin was administered intravenously at a dose of 25 mg/m^2 on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

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

Dosage and administration details:

Placebo matching bevacizumab was administered intravenously on Day 1 of each 21-day cycle after atezolizumab.

Arm title	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev

Arm description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

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

Dosage and administration details:

Atezolizumab was administered intravenously at a fixed dose of 1200 mg on Day 1 of each 21-day cycle.

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

Dosage and administration details:

Gemcitabine was administered intravenously at a dose of 1000 mg/m^2 on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

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

Dosage and administration details:

Cisplatin was administered intravenously at a dose of 25 mg/m^2 on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

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

Dosage and administration details:

Bevacizumab was administered at a dose of 15 mg/kg intravenously on Day 1 of each 21-day cycle after atezolizumab.

Number of subjects in period 1	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev
Started	83	79
Completed	0	0
Not completed	83	79
Adverse event, serious fatal	31	24
Consent withdrawn by subject	2	5
Ongoing in study	48	50
Progressive Disease	1	-
Symptomatic Deterioration	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO

Reporting group description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received placebo matching bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

Reporting group title	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev

Reporting group description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

Reporting group values	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev	Total
Number of subjects	83	79	162
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	38	51	89
From 65-84 years	45	28	73
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	63.0	59.6	
standard deviation	± 9.8	± 9.9	-
Sex: Female, Male Units:			
Female	45	30	75
Male	38	49	87
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	35	37	72
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	2
White	46	41	87
More than one race	0	0	0

Unknown or Not Reported	1	0	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	2
Not Hispanic or Latino	82	78	160
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO

Reporting group description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received placebo matching bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

Reporting group title	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev

Reporting group description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS is defined as the time from randomization to the first occurrence of disease progression as determined by the investigator according to RECIST v1.1 or death from any cause (whichever occurs first)

End point type	Primary

End point timeframe:

Randomization to the first occurrence of disease progression as determined by the investigator according to RECIST v1.1 or death from any cause (whichever occurs first)(up to approximately 14 months)

End point values	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	79		
Units: Months				
median (confidence interval 95%)	7.92 (6.18 to 8.41)	8.35 (6.83 to 9.96)		

Statistical analyses

Statistical analysis title	PFS Statistical Analysis

Statistical analysis description:

Stratified analysis. Stratification factors are: Location of primary tumor (iCCA vs. eCCA vs. GBC), Geographic region (Asia vs. Rest of the World).

Comparison groups	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO v Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev

Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.14

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS is defined as the time from randomization to death from any cause. 999999=not estimable.

End point type	Secondary

End point timeframe:

Randomization to death from any cause (up to approximately 14 months)

End point values	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	79		
Units: Months				
median (confidence interval 95%)	11.37 (10.61 to 999999)	999999 (10.97 to 999999)		

Statistical analyses

Statistical analysis title	OS Statistical Analysis

Statistical analysis description:

Stratified analysis. Stratification factors are: Location of primary tumor (iCCA vs. eCCA vs. GBC), Geographic region (Asia vs. Rest of the World).

Comparison groups	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO v Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.27

Secondary: Confirmed Objective Response Rate (ORR)

End point title	Confirmed Objective Response Rate (ORR)

End point description:

Confirmed ORR is defined as the proportion of participants with Complete Response (CR) or Partial Response (PR) on two consecutive occasions >=4 weeks apart, as determined by the investigator according to RECIST v1.1.

End point type	Secondary

End point timeframe:

Randomization up to approximately 14 months

End point values	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	79		
Units: Percentage of participants				
number (not applicable)	25.3	24.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR is defined as the time from the first occurrence of a confirmed objective response to disease progression as determined by the investigator according to RECIST v1.1 or death from any cause (whichever occurs first). 999999=not estimable.

End point type	Secondary

End point timeframe:

First occurrence of a confirmed objective response to disease progression as determined by the investigator according to RECIST v1.1 or death from any cause (whichever occurs first)(up to approximately 14 months)

End point values	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	19		
Units: Months				
median (confidence interval 95%)	5.78 (4.27 to 6.70)	999999 (6.44 to 999999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

DCR is defined as the proportion of participants with a CR or a PR on two consecutive occasions >= 4 weeks apart or SD with a minimum duration of 9weeks, as determined by the investigator according to RECIST v1.1

End point type	Secondary

End point timeframe:

Randomization up to approximately 14 months

End point values	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	79		
Units: Percentage of participants				
number (not applicable)	75.9	78.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Confirmed Deterioration (TTCD)

End point title	Time to Confirmed Deterioration (TTCD)

End point description:

TTCD in patient-reported physical functioning, role functioning, and quality of life, as measured by the respective scales of the EORTC QLQ-C30 and/or EORTC IL77, and defined as the time from randomization to the first clinically meaningful deterioration that is either maintained for two consecutive assessments or followed by death from any cause within 3 weeks. 999999=not estimable.

End point type	Secondary

End point timeframe:

Randomization to the first clinically meaningful deterioration (up to approximately 14 months)

End point values	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83	79		
Units: Months				
median (confidence interval 95%)				
Quality of Life	6.28 (3.06 to 999999)	2.79 (1.58 to 5.32)		
Physical Function Scale	3.29 (1.87 to 10.58)	6.21 (4.63 to 999999)		
Role Function Scale	3.52 (2.20 to 8.51)	4.24 (2.10 to 6.28)		

Statistical analyses

Statistical analysis title	Quality of Life Statistical Analysis

Statistical analysis description:

Stratified analysis. Stratification factors are: Location of primary tumor (iCCA vs. eCCA vs. GBC), Geographic region (Asia vs. Rest of the World).

Comparison groups	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO v Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	2.63

Statistical analysis title	Role Function Scale Statistical Analysis

Statistical analysis description:

Stratified analysis. Stratification factors are: Location of primary tumor (iCCA vs. eCCA vs. GBC), Geographic region (Asia vs. Rest of the World).

Comparison groups	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO v Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev

Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.85

Statistical analysis title	Physical Function Scale Statistical Analysis
Statistical analysis description:	
Stratified analysis. Stratification factors are: Location of primary tumor (iCCA vs. eCCA vs. GBC), Geographic region (Asia vs. Rest of the World).	
Comparison groups	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO v Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev
Number of subjects included in analysis	162
Analysis specification	Pre-specified
Analysis type	superiority
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.36

Secondary: Percentage of Participants With Adverse Events

End point title	Percentage of Participants With Adverse Events
End point description:	
End point type	Secondary
End point timeframe:	
Randomization up to approximately 3-5 years	

End point values	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[1]	0[2]		
Units: Percentage of participants				

Notes:

[1] - To be reported after end of study.

[2] - To be reported after end of study.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Atezolizumab

End point title	Serum Concentration of Atezolizumab

End point description:

Serum concentration of atezolizumab at specified timepoints. Note: 999999= below the level of detection.

End point type	Secondary

End point timeframe:

Pre-Dose on Day 1 of Cycles 1, 2, 3, 4, 8, 12, and 16, and Post Dose Day 1 of Cycle 1 (cycle length=21 days)

End point values	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	78		
Units: µg/ mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1 Pre-Dose (n=74, 78)	999999 (± 999999)	999999 (± 999999)		
Cycle 1 Day 1 Post Dose (n=75, 80)	416 (± 173)	411 (± 73.8)		
Cycle 2 Day 1 Pre-Dose (n=75, 78)	85.0 (± 71.7)	79.4 (± 46.1)		
Cycle 3 Day 1 Pre-Dose (n=72, 74)	129 (± 83.5)	118 (± 41.4)		
Cycle 4 Day 1 Pre-Dose (n=69, 64)	153 (± 74.8)	155 (± 50.6)		
Cycle 8 Day 1 Pre-Dose (n=54, 51)	224 (± 126)	200 (± 100)		
Cycle 12 Day 1 Pre-Dose (n=31, 28)	223 (± 103)	210 (± 76.4)		
Cycle 16 Day 1 Pre-Dose (n=8, 6)	230 (± 71.6)	174 (± 64.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of ADAs to Atezolizumab

End point title	Incidence of ADAs to Atezolizumab

End point description:	
End point type	Secondary
End point timeframe:	
At pre-defined intervals from administration of study drug up to approximately 3-5 years	

End point values	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	0[4]		
Units: Percentage of participants				

Notes:

[3] - There is no data because the samples were not measured.

[4] - There is no data because the samples were not measured.

Statistical analyses

No statistical analyses for this end point

Secondary: Prevalence of ADAs to Atezolizumab

End point title	Prevalence of ADAs to Atezolizumab
End point description:	
End point type	Secondary
End point timeframe:	
Baseline	

End point values	Arm B: Atezo+PBO+CisGem, followed by Atezo+PBO	Arm A: Atezo+Bev+CisGem, followed by Atezo+Bev		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: Percentage of participants				

Notes:

[5] - There is no data because the samples were not measured.

[6] - There is no data because the samples were not measured.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the first study drug until the data cut-off on 16 May 2022 (up to approximately 14 months)	
Adverse event reporting additional description: Safety-evaluable population included all randomized participants who receive any amount of any component of protocol treatment.	
Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Atezolizumab+Placebo+Cisplatin+Gemcitabine

Reporting group description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received placebo matching bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

Reporting group title	Atezolizumab+Bevacizumab+Cisplatin+Gemcitabine

Reporting group description:

Participants received atezolizumab intravenously on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, and clinical status. Participants received bevacizumab intravenously on Day 1 of each 21-day cycle. Participants received cisplatin intravenously followed by gemcitabine on Days 1 and 8 of each 21-day cycle for Cycles 1-8.

Serious adverse events	Atezolizumab+Placebo+Cisplatin+Gemcitabine	Atezolizumab+Bevacizumab+Cisplatin+Gemcitabine	
Total subjects affected by serious adverse events			
subjects affected / exposed	42 / 81 (51.85%)	36 / 78 (46.15%)	
number of deaths (all causes)	31	24	
number of deaths resulting from adverse events	1	1	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			

subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	2 / 81 (2.47%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	5 / 81 (6.17%)	3 / 78 (3.85%)	
occurrences causally related to treatment / all	1 / 10	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	2 / 81 (2.47%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Asthenia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatic obstruction			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 81 (1.23%)	2 / 78 (2.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 81 (2.47%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood culture positive			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	2 / 81 (2.47%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
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			
Head injury			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebellar infarction			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem infarction			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Neutropenia				
subjects affected / exposed	2 / 81 (2.47%)	2 / 78 (2.56%)		
occurrences causally related to treatment / all	3 / 3	3 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
Febrile neutropenia				
subjects affected / exposed	0 / 81 (0.00%)	2 / 78 (2.56%)		
occurrences causally related to treatment / all	0 / 0	2 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Anaemia				
subjects affected / exposed	6 / 81 (7.41%)	1 / 78 (1.28%)		
occurrences causally related to treatment / all	6 / 6	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Thrombocytopenia				
subjects affected / exposed	2 / 81 (2.47%)	2 / 78 (2.56%)		
occurrences causally related to treatment / all	2 / 2	3 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Abdominal pain upper				
subjects affected / exposed	2 / 81 (2.47%)	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 2	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Colitis				
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Diarrhoea				
subjects affected / exposed	1 / 81 (1.23%)	1 / 78 (1.28%)		
occurrences causally related to treatment / all	1 / 1	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Duodenal perforation				

subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Duodenal ulcer				
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Enterocolitis				
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Haematemesis				
subjects affected / exposed	0 / 81 (0.00%)	2 / 78 (2.56%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Gastrointestinal obstruction				
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Intestinal perforation				
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Nausea				
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Large intestinal stenosis				

subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Hepatobiliary disorders			
Biliary dilatation			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disease			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	1 / 81 (1.23%)	2 / 78 (2.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			

subjects affected / exposed	4 / 81 (4.94%)	2 / 78 (2.56%)	
occurrences causally related to treatment / all	1 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary obstruction			
subjects affected / exposed	3 / 81 (3.70%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	2 / 81 (2.47%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephropathy toxic			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	2 / 81 (2.47%)	3 / 78 (3.85%)	
occurrences causally related to treatment / all	0 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 81 (1.23%)	2 / 78 (2.56%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Anal abscess			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			

subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	3 / 81 (3.70%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	2 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Recurrent pyogenic cholangitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (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	2 / 81 (2.47%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metabolism and nutrition disorders			
Hypokalaemia			

subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	1 / 81 (1.23%)	0 / 78 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	0 / 81 (0.00%)	1 / 78 (1.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Atezolizumab+Placebo+Cisplatin+Gemcitabine	Atezolizumab+Bevacizumab+Cisplatin+Gemcitabine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 81 (98.77%)	77 / 78 (98.72%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	15 / 81 (18.52%)	29 / 78 (37.18%)	
occurrences (all)	16	35	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	16 / 81 (19.75%)	14 / 78 (17.95%)	
occurrences (all)	33	27	
Fatigue			

subjects affected / exposed	18 / 81 (22.22%)	20 / 78 (25.64%)	
occurrences (all)	22	28	
Oedema peripheral			
subjects affected / exposed	7 / 81 (8.64%)	5 / 78 (6.41%)	
occurrences (all)	8	5	
Pyrexia			
subjects affected / exposed	20 / 81 (24.69%)	13 / 78 (16.67%)	
occurrences (all)	41	25	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	8 / 81 (9.88%)	3 / 78 (3.85%)	
occurrences (all)	9	3	
Epistaxis			
subjects affected / exposed	1 / 81 (1.23%)	10 / 78 (12.82%)	
occurrences (all)	2	11	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	7 / 81 (8.64%)	1 / 78 (1.28%)	
occurrences (all)	7	1	
Investigations			
Blood creatinine increased			
subjects affected / exposed	11 / 81 (13.58%)	6 / 78 (7.69%)	
occurrences (all)	13	6	
Blood bilirubin increased			
subjects affected / exposed	7 / 81 (8.64%)	7 / 78 (8.97%)	
occurrences (all)	10	7	
Blood alkaline phosphatase increased			
subjects affected / exposed	5 / 81 (6.17%)	4 / 78 (5.13%)	
occurrences (all)	7	8	
Aspartate aminotransferase increased			
subjects affected / exposed	16 / 81 (19.75%)	7 / 78 (8.97%)	
occurrences (all)	19	11	
Alanine aminotransferase increased			
subjects affected / exposed	13 / 81 (16.05%)	9 / 78 (11.54%)	
occurrences (all)	20	12	
C-reactive protein increased			

subjects affected / exposed	5 / 81 (6.17%)	1 / 78 (1.28%)	
occurrences (all)	7	1	
Lymphocyte count decreased			
subjects affected / exposed	7 / 81 (8.64%)	7 / 78 (8.97%)	
occurrences (all)	17	17	
Neutrophil count decreased			
subjects affected / exposed	32 / 81 (39.51%)	38 / 78 (48.72%)	
occurrences (all)	76	93	
Platelet count decreased			
subjects affected / exposed	22 / 81 (27.16%)	22 / 78 (28.21%)	
occurrences (all)	47	46	
Weight decreased			
subjects affected / exposed	6 / 81 (7.41%)	9 / 78 (11.54%)	
occurrences (all)	6	9	
Weight increased			
subjects affected / exposed	4 / 81 (4.94%)	5 / 78 (6.41%)	
occurrences (all)	4	5	
White blood cell count decreased			
subjects affected / exposed	13 / 81 (16.05%)	15 / 78 (19.23%)	
occurrences (all)	33	32	
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 81 (3.70%)	5 / 78 (6.41%)	
occurrences (all)	3	5	
Headache			
subjects affected / exposed	5 / 81 (6.17%)	7 / 78 (8.97%)	
occurrences (all)	8	7	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	17 / 81 (20.99%)	17 / 78 (21.79%)	
occurrences (all)	31	38	
Anaemia			
subjects affected / exposed	50 / 81 (61.73%)	38 / 78 (48.72%)	
occurrences (all)	77	59	
Thrombocytopenia			

subjects affected / exposed	6 / 81 (7.41%)	7 / 78 (8.97%)	
occurrences (all)	12	18	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	5 / 81 (6.17%)	5 / 78 (6.41%)	
occurrences (all)	5	6	
Abdominal pain			
subjects affected / exposed	12 / 81 (14.81%)	13 / 78 (16.67%)	
occurrences (all)	13	14	
Diarrhoea			
subjects affected / exposed	11 / 81 (13.58%)	13 / 78 (16.67%)	
occurrences (all)	12	21	
Constipation			
subjects affected / exposed	21 / 81 (25.93%)	27 / 78 (34.62%)	
occurrences (all)	23	35	
Stomatitis			
subjects affected / exposed	4 / 81 (4.94%)	7 / 78 (8.97%)	
occurrences (all)	4	7	
Nausea			
subjects affected / exposed	32 / 81 (39.51%)	32 / 78 (41.03%)	
occurrences (all)	43	50	
Haemorrhoids			
subjects affected / exposed	0 / 81 (0.00%)	4 / 78 (5.13%)	
occurrences (all)	0	4	
Dyspepsia			
subjects affected / exposed	7 / 81 (8.64%)	2 / 78 (2.56%)	
occurrences (all)	7	2	
Vomiting			
subjects affected / exposed	11 / 81 (13.58%)	15 / 78 (19.23%)	
occurrences (all)	11	22	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 81 (2.47%)	4 / 78 (5.13%)	
occurrences (all)	2	4	
Pruritus			

subjects affected / exposed	6 / 81 (7.41%)	6 / 78 (7.69%)	
occurrences (all)	7	8	
Rash			
subjects affected / exposed	8 / 81 (9.88%)	10 / 78 (12.82%)	
occurrences (all)	8	14	
Urticaria			
subjects affected / exposed	1 / 81 (1.23%)	4 / 78 (5.13%)	
occurrences (all)	1	4	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	8 / 81 (9.88%)	13 / 78 (16.67%)	
occurrences (all)	8	15	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	5 / 81 (6.17%)	4 / 78 (5.13%)	
occurrences (all)	5	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 81 (4.94%)	7 / 78 (8.97%)	
occurrences (all)	5	8	
Back pain			
subjects affected / exposed	5 / 81 (6.17%)	6 / 78 (7.69%)	
occurrences (all)	5	10	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	5 / 81 (6.17%)	4 / 78 (5.13%)	
occurrences (all)	5	4	
COVID-19			
subjects affected / exposed	9 / 81 (11.11%)	8 / 78 (10.26%)	
occurrences (all)	9	8	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	11 / 81 (13.58%)	7 / 78 (8.97%)	
occurrences (all)	12	10	
Decreased appetite			

subjects affected / exposed	14 / 81 (17.28%)	15 / 78 (19.23%)	
occurrences (all)	15	16	
Hyperglycaemia			
subjects affected / exposed	5 / 81 (6.17%)	1 / 78 (1.28%)	
occurrences (all)	5	1	
Hypoalbuminaemia			
subjects affected / exposed	6 / 81 (7.41%)	8 / 78 (10.26%)	
occurrences (all)	6	8	
Hypokalaemia			
subjects affected / exposed	11 / 81 (13.58%)	6 / 78 (7.69%)	
occurrences (all)	12	7	
Hypomagnesaemia			
subjects affected / exposed	6 / 81 (7.41%)	10 / 78 (12.82%)	
occurrences (all)	6	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 October 2020	Protocol has been amended to include sensitivity analysis to assess the robustness of the primary progression-free survival analysis. A sensitivity analysis will be performed by incorporating an additional censoring rule for participants who take new anti-cancer therapy prior to occurrence of radiographic progression. These participants will be censored at the last tumor assessment before the start of the new treatment, regardless of progression or death afterwards.
03 March 2021	Protocol has been amended to include updates to the exclusion criteria around symptomatic and asymptomatic brain metastasis. Also, participants with large centrally located pulmonary metastases; clear tumor infiltration into the thoracic great vessels seen on imaging; and clear cavitation of pulmonary lesions seen on imaging will be excluded from this study. The order of administration of cisplatin and gemcitabine has been clarified. The list of identified risks for atezolizumab have been revised to include severe cutaneous adverse reactions. Language has been added to clarify that hemophagocytic lymphohistiocytosis and macrophage activation syndrome are considered potential risks for atezolizumab.
27 September 2022	Protocol has been amended to add a final overall survival analysis. The timing of the patient-reported outcome assessments has been clarified.
03 February 2023	Protocol has been amended to include pericardial disorders, myelitis, and facial paresis in the list of identified risks for atezolizumab. Hemophagocytic lymphohistiocytosis has been updated from a potential risk to an identified risk associated with atezolizumab.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported