



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	v2
This version publication date	14 July 2023
First version publication date	27 May 2023
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	GO42661
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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
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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	Investigator, Subject

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/m² 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/m² 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
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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/m² 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/m² 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
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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
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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: 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: 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	0 ^[1]	0 ^[2]		
Units: Months				
median (confidence interval 95%)	(to)	(to)		

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: Duration of Response (DOR)

End point title	Duration of Response (DOR)
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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
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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: Time to Confirmed Deterioration (TTCD)

End point title	Time to Confirmed Deterioration (TTCD)
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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: 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: Percentage of Participants With Adverse Events

End point title	Percentage of Participants With Adverse Events
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End point description:

End point type	Secondary
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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 ^[3]	0 ^[4]		
Units: Percentage of participants				

Notes:

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

[4] - 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
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End point description:

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

End point type	Secondary
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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 ^[5]	0 ^[6]		
Units: Percentage of participants				

Notes:

[5] - No data were collected because the study was discontinued before any measurements were completed.

[6] - No data were collected because the study was discontinued before any measurements were completed.

Statistical analyses

No statistical analyses for this end point

Secondary: Prevalence of ADAs to Atezolizumab

End point title	Prevalence of ADAs to Atezolizumab
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End point description:

End point type	Secondary
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End point timeframe:

Baseline

End point values	Arm B: Atezo+PBO+Cis sGem, followed by Atezo+PBO	Arm A: Atezo+Bev+Cis Gem, followed by Atezo+Bev		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[7]	0 ^[8]		
Units: Percentage of participants				

Notes:

[7] - No data were collected because the study was discontinued before any measurements were completed.

[8] - No data were collected because the study was discontinued before any measurements were completed.

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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	Atezolizumab+Bevacizumab+Cisplatin+Gemcitabine
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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 title	Atezolizumab+Placebo+Cisplatin+Gemcitabine
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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.

Serious adverse events	Atezolizumab+Bevacizumab+Cisplatin+Gemcitabine	Atezolizumab+Placebo+Cisplatin+Gemcitabine	
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 78 (46.15%)	42 / 81 (51.85%)	
number of deaths (all causes)	24	31	
number of deaths resulting from adverse events	1	1	
Vascular disorders			
Thrombosis			
subjects affected / exposed	0 / 78 (0.00%)	2 / 81 (2.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 78 (1.28%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			

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

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

subjects affected / exposed	1 / 78 (1.28%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	1 / 78 (1.28%)	2 / 81 (2.47%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood culture positive			
subjects affected / exposed	1 / 78 (1.28%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	1 / 78 (1.28%)	0 / 81 (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	0 / 78 (0.00%)	2 / 81 (2.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 78 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Spinal compression fracture			
subjects affected / exposed	0 / 78 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 78 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

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

Neutropenia			
subjects affected / exposed	2 / 78 (2.56%)	2 / 81 (2.47%)	
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	2 / 78 (2.56%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 78 (1.28%)	6 / 81 (7.41%)	
occurrences causally related to treatment / all	1 / 1	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	2 / 78 (2.56%)	2 / 81 (2.47%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 78 (1.28%)	1 / 81 (1.23%)	
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	0 / 78 (0.00%)	2 / 81 (2.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

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

subjects affected / exposed	1 / 78 (1.28%)	0 / 81 (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 / 78 (1.28%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 78 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary dilatation			
subjects affected / exposed	1 / 78 (1.28%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary obstruction			
subjects affected / exposed	0 / 78 (0.00%)	3 / 81 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	2 / 78 (2.56%)	4 / 81 (4.94%)	
occurrences causally related to treatment / all	0 / 3	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	0 / 78 (0.00%)	1 / 81 (1.23%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 78 (1.28%)	0 / 81 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disease			

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

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

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

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

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

Non-serious adverse events	Atezolizumab+Bevacizumab+Cisplatin+Gemcitabine	Atezolizumab+Placebo+Cisplatin+Gemcitabine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	77 / 78 (98.72%)	80 / 81 (98.77%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	29 / 78 (37.18%)	15 / 81 (18.52%)	
occurrences (all)	35	16	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	13 / 78 (16.67%)	20 / 81 (24.69%)	
occurrences (all)	25	41	
Oedema peripheral			

subjects affected / exposed occurrences (all)	5 / 78 (6.41%) 5	7 / 81 (8.64%) 8	
Fatigue subjects affected / exposed occurrences (all)	20 / 78 (25.64%) 28	18 / 81 (22.22%) 22	
Asthenia subjects affected / exposed occurrences (all)	14 / 78 (17.95%) 27	16 / 81 (19.75%) 33	
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	10 / 78 (12.82%) 11	1 / 81 (1.23%) 2	
Cough subjects affected / exposed occurrences (all)	3 / 78 (3.85%) 3	8 / 81 (9.88%) 9	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 78 (1.28%) 1	7 / 81 (8.64%) 7	
Investigations White blood cell count decreased subjects affected / exposed occurrences (all)	15 / 78 (19.23%) 32	13 / 81 (16.05%) 33	
Weight increased subjects affected / exposed occurrences (all)	5 / 78 (6.41%) 5	4 / 81 (4.94%) 4	
Weight decreased subjects affected / exposed occurrences (all)	9 / 78 (11.54%) 9	6 / 81 (7.41%) 6	
Platelet count decreased subjects affected / exposed occurrences (all)	22 / 78 (28.21%) 46	22 / 81 (27.16%) 47	
Neutrophil count decreased subjects affected / exposed occurrences (all)	38 / 78 (48.72%) 93	32 / 81 (39.51%) 76	
Lymphocyte count decreased			

subjects affected / exposed	7 / 78 (8.97%)	7 / 81 (8.64%)	
occurrences (all)	17	17	
C-reactive protein increased			
subjects affected / exposed	1 / 78 (1.28%)	5 / 81 (6.17%)	
occurrences (all)	1	7	
Blood creatinine increased			
subjects affected / exposed	6 / 78 (7.69%)	11 / 81 (13.58%)	
occurrences (all)	6	13	
Blood bilirubin increased			
subjects affected / exposed	7 / 78 (8.97%)	7 / 81 (8.64%)	
occurrences (all)	7	10	
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 78 (5.13%)	5 / 81 (6.17%)	
occurrences (all)	8	7	
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 78 (8.97%)	16 / 81 (19.75%)	
occurrences (all)	11	19	
Alanine aminotransferase increased			
subjects affected / exposed	9 / 78 (11.54%)	13 / 81 (16.05%)	
occurrences (all)	12	20	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 78 (6.41%)	3 / 81 (3.70%)	
occurrences (all)	5	3	
Headache			
subjects affected / exposed	7 / 78 (8.97%)	5 / 81 (6.17%)	
occurrences (all)	7	8	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	7 / 78 (8.97%)	6 / 81 (7.41%)	
occurrences (all)	18	12	
Neutropenia			
subjects affected / exposed	17 / 78 (21.79%)	17 / 81 (20.99%)	
occurrences (all)	38	31	
Anaemia			

subjects affected / exposed occurrences (all)	38 / 78 (48.72%) 59	50 / 81 (61.73%) 77	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	15 / 78 (19.23%)	11 / 81 (13.58%)	
occurrences (all)	22	11	
Stomatitis			
subjects affected / exposed	7 / 78 (8.97%)	4 / 81 (4.94%)	
occurrences (all)	7	4	
Nausea			
subjects affected / exposed	32 / 78 (41.03%)	32 / 81 (39.51%)	
occurrences (all)	50	43	
Haemorrhoids			
subjects affected / exposed	4 / 78 (5.13%)	0 / 81 (0.00%)	
occurrences (all)	4	0	
Dyspepsia			
subjects affected / exposed	2 / 78 (2.56%)	7 / 81 (8.64%)	
occurrences (all)	2	7	
Diarrhoea			
subjects affected / exposed	13 / 78 (16.67%)	11 / 81 (13.58%)	
occurrences (all)	21	12	
Constipation			
subjects affected / exposed	27 / 78 (34.62%)	21 / 81 (25.93%)	
occurrences (all)	35	23	
Abdominal pain			
subjects affected / exposed	13 / 78 (16.67%)	12 / 81 (14.81%)	
occurrences (all)	14	13	
Ascites			
subjects affected / exposed	5 / 78 (6.41%)	5 / 81 (6.17%)	
occurrences (all)	6	5	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	6 / 78 (7.69%)	6 / 81 (7.41%)	
occurrences (all)	8	7	
Alopecia			

subjects affected / exposed occurrences (all)	4 / 78 (5.13%) 4	2 / 81 (2.47%) 2	
Rash subjects affected / exposed occurrences (all)	10 / 78 (12.82%) 14	8 / 81 (9.88%) 8	
Urticaria subjects affected / exposed occurrences (all)	4 / 78 (5.13%) 4	1 / 81 (1.23%) 1	
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	13 / 78 (16.67%) 15	8 / 81 (9.88%) 8	
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	4 / 78 (5.13%) 4	5 / 81 (6.17%) 5	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	7 / 78 (8.97%) 8	4 / 81 (4.94%) 5	
Back pain subjects affected / exposed occurrences (all)	6 / 78 (7.69%) 10	5 / 81 (6.17%) 5	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	8 / 78 (10.26%) 8	9 / 81 (11.11%) 9	
Urinary tract infection subjects affected / exposed occurrences (all)	4 / 78 (5.13%) 4	5 / 81 (6.17%) 5	
Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all)	6 / 78 (7.69%) 7	11 / 81 (13.58%) 12	
Hypomagnesaemia			

subjects affected / exposed	10 / 78 (12.82%)	6 / 81 (7.41%)	
occurrences (all)	12	6	
Hyponatraemia			
subjects affected / exposed	7 / 78 (8.97%)	11 / 81 (13.58%)	
occurrences (all)	10	12	
Hypoalbuminaemia			
subjects affected / exposed	8 / 78 (10.26%)	6 / 81 (7.41%)	
occurrences (all)	8	6	
Hyperglycaemia			
subjects affected / exposed	1 / 78 (1.28%)	5 / 81 (6.17%)	
occurrences (all)	1	5	
Decreased appetite			
subjects affected / exposed	15 / 78 (19.23%)	14 / 81 (17.28%)	
occurrences (all)	16	15	

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