Clinical trial results:
A Phase III, Multicenter, Randomized, Open-Label, Controlled Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Atezolizumab Given in Combination With Cabozantinib Versus Docetaxel Monotherapy in Patients With Metastatic Non-Small Lung Cancer Previously Treated With an Anti-PD-L1/PD-1 Antibody and Platinum-Containing Chemotherapy

Summary

EudraCT number	2020-000100-11
Trial protocol	DE PT BE GB GR PL FR IT
Global end of trial date	

Results information

Result version number	v2
This version publication date	13 April 2024
First version publication date	14 October 2023
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	GO41892

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04471428
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland,
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, + 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, + 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	28 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 September 2022
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to evaluate the efficacy, safety, and pharmacokinetics of atezolizumab when given in combination with cabozantinib (Atezo + Cabo) compared with docetaxel monotherapy in subjects with metastatic non-small cell lung cancer (NSCLC), with no sensitizing endothelial growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) translocation, who have progressed on prior treatment with both anti-PD-L1/PD-1 antibody and platinum-containing chemotherapy.

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	01 October 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	France: 27
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	Greece: 31
Country: Number of subjects enrolled	Italy: 45
Country: Number of subjects enrolled	Japan: 23
Country: Number of subjects enrolled	Korea, Republic of: 61
Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Portugal: 16
Country: Number of subjects enrolled	Russian Federation: 24
Country: Number of subjects enrolled	United States: 29
Worldwide total number of subjects	366
EEA total number of subjects	210

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)	178
From 65 to 84 years	187
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants are enrolled in the study at study centers in 15 countries. The study is ongoing.

Pre-assignment

Screening details:

Of the 366 participants, 180 participants were randomized to receive Docetaxel monotherapy whereas 186 participants were randomized to receive Atezolizumab and Cabozantinib combination therapy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Docetaxel

Arm description:

Participants received docetaxel intravenously at a starting dose of 75mg/m^2 on Day 1 of each 21-day cycle.

Arm type	Active comparator
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	RO0647746
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel was administered on Day 1 of each 21-day cycle.

Arm title	Atezolizumab + Cabozantinib

Arm description:

Participants received atezolizumab intravenously at a fixed dose of 1200 mg on Day 1 of each 21-day cycle. Cabozantinib was administered orally, once daily at a dose of 40 mg in each 21-day cycle.

Arm type	Experimental
Investigational medicinal product name	Cabozantinib
Investigational medicinal product code	RO7047650
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Cabozantinib was administered orally, once daily at a dose of 40 mg in each 21-day cycle.

Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	RO5541267
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1200 mg atezolizumab on Day 1 of each 21-day cycle

Number of subjects in period 1	Docetaxel	Atezolizumab + Cabozantinib
Started	180	186
Completed	0	0
Not completed	180	186
Physician decision	-	1
Death	106	114
Reason Not Specified	-	2
Withdrawal by Subject	29	1
Ongoing in the study	45	68

Baseline characteristics

Reporting groups	
Reporting group title	Docetaxel
Reporting group description:	
Participants received docetaxel intravenously at a starting dose of 75mg/m^2 on Day 1 of each 21-day cycle.	
Reporting group title	Atezolizumab + Cabozantinib
Reporting group description:	
Participants received atezolizumab intravenously at a fixed dose of 1200 mg on Day 1 of each 21-day cycle. Cabozantinib was administered orally, once daily at a dose of 40 mg in each 21-day cycle.	

Reporting group values	Docetaxel	Atezolizumab + Cabozantinib	Total
Number of subjects	180	186	366
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)	83	95	178
From 65-84 years	96	91	187
85 years and over	1	0	1
Age Continuous Units: years			
arithmetic mean	64.4	63.8	
standard deviation	± 9.4	± 9.5	-
Sex: Female, Male Units: participants			
Female	53	52	105
Male	127	134	261
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	53	41	94
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	2	3
White	111	130	241
More than one race	0	0	0
Unknown or Not Reported	15	13	28
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	7	4	11
Not Hispanic or Latino	158	164	322
Not Stated	12	15	27

Unknown	3	3	6

End points

End points reporting groups

Reporting group title	Docetaxel
Reporting group description:	
Participants received docetaxel intravenously at a starting dose of 75mg/m^2 on Day 1 of each 21-day cycle.	
Reporting group title	Atezolizumab + Cabozantinib
Reporting group description:	
Participants received atezolizumab intravenously at a fixed dose of 1200 mg on Day 1 of each 21-day cycle. Cabozantinib was administered orally, once daily at a dose of 40 mg in each 21-day cycle.	

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS was defined as time from randomization to death from any cause. Participants alive at time of analysis were censored at date when they were last known to be alive as documented by investigator. Kaplan-Meier method was used to estimate median. 95% CI for median was computed using method of Brookmeyer and Crowley. Intent-to-treat (ITT) population included all randomised participants, whether or not the participant received the assigned treatment.	
End point type	Primary
End point timeframe:	
Up to approximately 24 months	

End point values	Docetaxel	Atezolizumab + Cabozantinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	186		
Units: months				
median (confidence interval 95%)	10.5 (8.6 to 13.0)	10.7 (8.8 to 12.3)		

Statistical analyses

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description:	
Unstratified Analysis	
Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4709
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.907

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.696
upper limit	1.182

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description:	
Stratified Analysis	
Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.3668
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.884
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.676
upper limit	1.156

Notes:

[1] - Stratification factors include histology, and prior NSCLC treatment regimens

Secondary: Progression-Free Survival (PFS) as Determined by Investigator

End point title	Progression-Free Survival (PFS) as Determined by Investigator

End point description:

PFS was defined as time from randomisation to first occurrence of disease progression, as determined by investigator according to RECIST v1.1, or death from any cause (whichever occurred first). Progressive disease(PD) was defined as at least 20% increase in sum of longest diameters(D) of target lesions, taking as reference smallest sum of longest D of target lesions recorded since treatment started, including screening, or appearance of 1 or more new lesions. Participants who were alive & did not experience disease progression at time of analysis, were censored on date of last tumor assessment. Participants with no post-baseline tumor assessment were censored at date of randomisation.ITT population included all randomised participants, whether or not participant received the assigned treatment.

End point type	Secondary

End point timeframe:

Up to approximately 24 months

End point values	Docetaxel	Atezolizumab + Cabozantinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	186		
Units: months				
median (confidence interval 95%)	4.0 (3.1 to 4.4)	4.6 (4.1 to 5.6)		

Statistical analyses

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description:	
Stratified Analysis	
Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.0079
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.735
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.585
upper limit	0.923

Notes:

[2] - Stratification factors include histology, and prior NSCLC treatment regimens

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description:	
Unstratified Analysis	
Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0061
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.731
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.583
upper limit	0.915

Secondary: Confirmed Objective Response Rate (ORR) as Determined by Investigator

End point title	Confirmed Objective Response Rate (ORR) as Determined by Investigator

End point description:

Confirmed ORR was defined as the percentage of participants with a complete response (CR) or partial response (PR) on two consecutive occasions >=4 weeks apart, as determined by the investigator according to RECIST v1.1. CR: disappearance of all target lesions. PR: at least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters. The ITT population included all randomised participants, whether or not the participant received the assigned treatment.

End point type	Secondary

End point timeframe:

Up to approximately 24 months

End point values	Docetaxel	Atezolizumab + Cabozantinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	186		
Units: percentage of participants				
number (confidence interval 95%)	13.3 (8.73 to 19.19)	11.8 (7.56 to 17.36)		

Statistical analyses

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib

Statistical analysis description:

Stratified analysis

Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.6846
Method	Chi-square with Schouten Correction
Parameter estimate	Difference in Response Rates
Point estimate	-1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.85
upper limit	5.84

Notes:

[3] - Stratification factors: histology, prior NSCLC treatment regimens

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib

Statistical analysis description:

Unstratified Analysis

Comparison groups	Docetaxel v Atezolizumab + Cabozantinib

Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.62

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description: Unstratified Analysis	
Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7216
Method	Chi-squared corrected
Parameter estimate	Difference in Response Rates
Point estimate	-1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.85
upper limit	5.84

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description: Stratified analysis	
Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority[4]
Parameter estimate	Odds ratio (OR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.63

Notes:

[4] - Stratification factors: histology, prior NSCLC treatment regimens

Secondary: Duration of response (DOR) as Determined by Investigator

End point title	Duration of response (DOR) as Determined by Investigator

End point description:

DOR for participants with confirmed ORR was defined as time from first occurrence of a documented objective response to disease progression (PD), as determined by investigator according to RECIST v1.1, or death from any cause (whichever occurred first). PD was defined as at least 20% increase in sum of longest diameters of target lesions, taking as reference smallest sum of longest diameters of target lesions recorded since treatment started, including screening, or appearance of one or more new lesions. Participants who had not progressed and who did not die at time of analysis were censored at the time of last tumor assessment date. Kaplan-Meier method was used to estimate median. 95% CI for median was computed using the method of Brookmeyer and Crowley (B&C). Participants in the ITT population who had a confirmed objective response (CR or PR) as determined by the investigator per RECIST v1.1 were included in the analysis.

End point type	Secondary

End point timeframe:

Up to approximately 24 months

End point values	Docetaxel	Atezolizumab + Cabozantinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	22		
Units: months				
median (confidence interval 95%)	4.30 (3.29 to 5.62)	5.55 (3.12 to 10.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: TTCD in Patient-Reported Global Health Status (GHS)

End point title	TTCD in Patient-Reported Global Health Status (GHS)

End point description:

TTCD analyses was performed for GHS/quality of life (QoL) items of EORTC QLQ-C30 on a 7-point scale with range = very poor to excellent. TTCD is time from date of randomization to 1st confirmed clinically meaningful decrease from baseline in GHS/QoL score held for at least 2 consecutive assessments/initial clinically meaningful decrease from baseline followed by death from any cause within 21 days/ until next tumor assessment, whichever occurs 1st. Change of >=10-point on GHS/QoL subs scale=clinically meaningful. Scores were transformed to 0-100 scale; high score =better health-related QoL. Kaplan-Meier method was used to estimate median. Participants without confirmed deterioration at time of analysis were censored at last time they were known to have not deteriorated. ITT population was used. Only responders were analysed in this endpoint. 9999=UL of 95% CI was not estimable as there were not enough events after median estimate to satisfy constraints required to calculate the UL.

End point type	Secondary

End point timeframe:

Up to approximately 24 months

End point values	Docetaxel	Atezolizumab + Cabozantinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	186		
Units: months				
median (confidence interval 95%)	14.1 (6.3 to 9999)	8.1 (5.6 to 14.5)		

Statistical analyses

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description: Unstratified Analysis	
Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1992
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.81

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description: Stratified Analysis	
Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.2408
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.79

Notes:

[5] - Stratification factors include histology, and prior NSCLC treatment regimens

Secondary: Time to Confirmed Deterioration (TTCD) in Patient-Reported Physical

Functioning (PF)	
End point title	Time to Confirmed Deterioration (TTCD) in Patient-Reported Physical Functioning (PF)

End point description:

TTCD for PF is time from date of randomization to 1st confirmed clinically meaningful decrease from baseline in PF score held for at least 2 assessments/initial clinically meaningful decrease from baseline followed by death from any cause within 21 days/until next tumor assessment, whichever occurs 1st. Score change >=of 10-point on European Organisation for Research and Treatment of Cancer Quality of Life-Core 30 Questionnaire (EORTC QLQ-C30) PF scale=clinically meaningful. Scores were averaged, transformed to 0-100 scale; where higher score=high/healthy level of functioning. Kaplan-Meier method was used to estimate median. 95% CI for median was computed using B&C method. ITT population was used. Participants without confirmed deterioration at time of analysis were censored at last time they were known to have not deteriorated. 9999=Upper limit (UL) of 95% CI was not estimable as there were not enough events after median estimate to satisfy constraints required to calculate the UL.

End point type	Secondary

End point timeframe:

Up to approximately 24 months

End point values	Docetaxel	Atezolizumab + Cabozantinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	186		
Units: months				
median (confidence interval 95%)	5.6 (4.0 to 9999)	7.7 (4.8 to 14.7)		

Statistical analyses

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib

Statistical analysis description:

Unstratified Analysis

Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3031
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.17

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib

Statistical analysis description:	
Stratified Analysis	
Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.27
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.16

Notes:

[6] - Stratification factors include histology, and prior NSCLC treatment regimens

Secondary: PFS Rates Assessed by Investigator

End point title	PFS Rates Assessed by Investigator

End point description:

PFS rates were defined as the percentage of participants alive and without progression as assessed by the investigator according to RECIST v1.1. PD was defined as at least a 20% increase in the sum of the longest diameters of target lesions, taking as reference the smallest sum of the longest diameters of the target lesions recorded since the treatment started, including screening, or the appearance of one or more new lesions. Participants with no post-baseline tumor assessment were censored at the date of randomization. ITT population is defined as all randomised participants, whether or not the participant received the assigned treatment. The overall number analyzed are the participants with data available for analyses.

End point type	Secondary

End point timeframe:

6 months and 1 year

End point values	Docetaxel	Atezolizumab + Cabozantinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	186		
Units: percentage of participants				
number (confidence interval 95%)				
At 6 months	23.66 (16.98 to 30.33)	39.51 (32.42 to 46.59)		
At 1 year	8.38 (3.95 to 12.80)	14.70 (9.43 to 19.97)		

Statistical analyses

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib

Statistical analysis description:

At 6 months

Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0014
Method	z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	15.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.12
upper limit	25.59

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description:	
At 1 year	
Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0719
Method	z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	6.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	13.21

Secondary: OS Rates

End point title	OS Rates

End point description:

Overall Survival (OS) rate is defined as the percentage of participants who were alive at 1 year and 2 years. Participants alive at the time of the analysis were censored at the date when they were last known to be alive as documented by the investigator. The ITT population is defined as all randomized participants, whether or not the participant received the assigned treatment. Here 99999 indicates that at the time of the analysis, there were no participants with 24 months or more of survival follow-up, therefore, survival rate at the 2-year timepoint was not estimable.

End point type	Secondary

End point timeframe:

At 1 and 2 years

End point values	Docetaxel	Atezolizumab + Cabozantinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	186		
Units: percentage of participants				
number (confidence interval 95%)				
At 1 year	44.12 (36.20 to 52.05)	43.27 (35.97 to 50.57)		
At 2 years	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description:	
At 1 year	
Comparison groups	Docetaxel v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8767
Method	z-test
Parameter estimate	Difference in Event Free Rate
Point estimate	-0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.63
upper limit	9.92

Secondary: Minimum Serum Concentration (Cmin) of Atezolizumab

End point title	Minimum Serum Concentration (Cmin) of Atezolizumab[7]

End point description:

The pharmacokinetic (PK)-evaluable population included all participants who received any dose of atezolizumab or cabozantinib and who had evaluable PK samples. Overall number analyzed is the number of participants with data available for analysis. Number analysed is the number of participants with data available for analysis at the specified timepoints. 9999= the data was not evaluable as all samples were Below Limit of Quantitation (BLQ)

End point type	Secondary

End point timeframe:

Predose on Day 1 of Cycles 1, 2, 3, 4, 8, 12 and 16 (each cycle is 21 days)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetics was analyzed for Atezolizumab for this endpoint.

End point values	Atezolizumab + Cabozantinib			
Subject group type	Reporting group			
Number of subjects analysed	185			
Units: microgram/milliliter (µg/ml)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 (n=146)	9999 (± 9999)			
Cycle 2 Day 1 (n=162)	96.8 (± 48.1)			
Cycle 3 Day 1 (n=140)	124 (± 104.4)			
Cycle 4 Day 1 (n=130)	167 (± 47.7)			
Cycle 8 Day 1 (n=70)	194 (± 62.4)			
Cycle 12 Day 1 (n=52)	233 (± 44.7)			
Cycle 16 Day 1 (n=40)	209 (± 56.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Adverse Events

End point title	Percentage of Participants With Adverse Events

End point description:

An adverse event is any untoward medical occurrence in a clinical investigation patient administered a pharmaceutical product, regardless of causal attribution. AEs were assessed using National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0 (NCI CTCAE, v5.0). Safety population included treated participants, defined as all randomised participants who received any amount of study drug.

End point type	Secondary

End point timeframe:

From signing the informed consent form up to the study completion date: 28 February 2024 (i.e., approximately 41 months)

End point values	Docetaxel	Atezolizumab + Cabozantinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: percentage of participants				
number (not applicable)				

Notes:

[8] - Data collection for this endpoint is ongoing and will be reported within 1 year of study completion.

[9] - Data collection for this endpoint is ongoing and will be reported within 1 year of study completion.

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Plasma Concentration (Cmin) of Cabozantinib

End point title	Minimum Plasma Concentration (Cmin) of Cabozantinib[10]

End point description:

The PK-evaluable population included all participants who received any dose of atezolizumab or cabozantinib and who had evaluable PK samples. Overall number analyzed is the number of participants with data available for analysis. Number analysed is the number of participants with data available for analysis at the specified timepoints. 9999= the data was not evaluable as all samples were BLQ.

End point type	Secondary

End point timeframe:

Predose on Day 1 of Cycles 1, 2, 3, 4, and 5 (each cycle is 21 days)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetics was analyzed for Cabozantinib only for this endpoint.

End point values	Atezolizumab + Cabozantinib			
Subject group type	Reporting group			
Number of subjects analysed	185			
Units: µg/ml				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 (n=173)	9999 (± 9999)			
Cycle 2 Day 1 (n=163)	0.746 (± 111.7)			
Cycle 3 Day 1 (n=138)	0.418 (± 640.7)			
Cycle 4 Day 1 (n=131)	0.469 (± 234.4)			
Cycle 5 Day 1 (n=110)	0.303 (± 402.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of Cabozantinib

End point title	Maximum Plasma Concentration (Cmax) of Cabozantinib[11]

End point description:

Cmax was not collected for this outcome measure because PK of cabozantinib was well characterized through the cabozantinib development for mono- therapy. An established population PK model for cabozantinib is available for the PK data from NCT04471428 (study GO41892). The PK data collected in the current study is sufficient for the population PK model to characterize the exposure of cabozantinib in this study.

End point type	Secondary

End point timeframe:

Predose on Day 1 of Cycles 1, 2, 3, 4, and 5 (each cycle is 21 days)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cabozantinib's PK was well studied through development of it's monotherapy, no need to measure Cmax.

End point values	Atezolizumab + Cabozantinib			
Subject group type	Reporting group			
Number of subjects analysed	0[12]			
Units: µg/ml				
geometric mean (geometric coefficient of variation)	()			

Notes:

[12] - Cabozantinib's PK was well studied through development of it's monotherapy, no need to measure Cmax.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Serum Concentration (Cmax) of Atezolizumab

End point title	Maximum Serum Concentration (Cmax) of Atezolizumab[13]

End point description:

The PK-evaluable population included all participants who received any dose of atezolizumab or cabozantinib and who had evaluable PK samples. Overall number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

30 min Post-dose on Day 1 of Cycle 1 (each cycle is 21 days)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetics was analyzed for Atezolizumab for this endpoint.

End point values	Atezolizumab + Cabozantinib			
Subject group type	Reporting group			
Number of subjects analysed	185			
Units: µg/ml				
geometric mean (geometric coefficient of variation)	450 (± 34.0)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Participants with Anti-Drug Antibodies (ADAs) to Atezolizumab[14]

End point description:

Safety population included treated participants, defined as all randomised participants who received any amount of study drug. Overall number analysed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Predose on Day 1 of Cycles 1,2,3,4,8,12 and 16 (each cycle is 21 days) and at post-treatment follow-up

visit (≤ 30 days after final dose)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Anti-Drug Antibodies (ADAs) were analyzed for Atezolizumab only for this endpoint.

End point values	Atezolizumab + Cabozantinib			
Subject group type	Reporting group			
Number of subjects analysed	177			
Units: participants				
ADA Prevalence at Baseline (n=177)	2			
ADA Incidence after treatment (n=173)	37			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From signing the informed consent form up to approximately 24 months. This study is still ongoing, and the AEs section will be updated 1 year after study completion.

Adverse event reporting additional description:

All-cause mortality was assessed in the ITT population, which included all randomized participants whether or not they received treatment. Serious adverse events and non-serious adverse events were assessed in the safety population, which included treated participants, defined as all randomized participants who received any amount of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Atezolizumab + Cabozantinib

Reporting group description:

Participants received atezolizumab intravenously at a fixed dose of 1200 mg on Day 1 of each 21-day cycle. Cabozantinib was administered orally, once daily at a dose of 40 mg in each 21-day cycle.

Reporting group title	Docetaxel

Reporting group description:

Participants received docetaxel intravenously at a starting dose of 75mg/m^2 on Day 1 of each 21-day cycle.

Serious adverse events	Atezolizumab + Cabozantinib	Docetaxel	
Total subjects affected by serious adverse events			
subjects affected / exposed	71 / 185 (38.38%)	58 / 167 (34.73%)	
number of deaths (all causes)	114	106	
number of deaths resulting from adverse events	4	1	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			

subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Mucosal inflammation			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	3 / 185 (1.62%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chest pain			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	5 / 185 (2.70%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	2 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			

subjects affected / exposed	3 / 185 (1.62%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Fatigue			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Condition aggravated			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Infusion related hypersensitivity reaction			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			

subjects affected / exposed	3 / 185 (1.62%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 185 (1.08%)	3 / 167 (1.80%)	
occurrences causally related to treatment / all	1 / 2	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	3 / 185 (1.62%)	5 / 167 (2.99%)	
occurrences causally related to treatment / all	3 / 3	4 / 5	
deaths causally related to treatment / all	2 / 2	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 185 (0.00%)	4 / 167 (2.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pulmonary infarction			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 185 (0.00%)	2 / 167 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary haemorrhage			
subjects affected / exposed	2 / 185 (1.08%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Bronchial fistula			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal inflammation			

subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 185 (0.00%)	2 / 167 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 185 (0.54%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocyte count decreased			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	2 / 185 (1.08%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumopericardium			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 185 (0.00%)	2 / 167 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			

subjects affected / exposed	0 / 185 (0.00%)	2 / 167 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Status epilepticus			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ataxia			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (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 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
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	1 / 185 (0.54%)	3 / 167 (1.80%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			

subjects affected / exposed	0 / 185 (0.00%)	8 / 167 (4.79%)	
occurrences causally related to treatment / all	0 / 0	9 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 185 (1.62%)	3 / 167 (1.80%)	
occurrences causally related to treatment / all	2 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 185 (1.62%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastritis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			

subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
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 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal disorder			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal fistula			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			

subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Hidradenitis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	3 / 185 (1.62%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Bladder disorder			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	2 / 185 (1.08%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscular weakness			

subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal sepsis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (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	10 / 185 (5.41%)	10 / 167 (5.99%)	
occurrences causally related to treatment / all	0 / 10	4 / 10	
deaths causally related to treatment / all	0 / 3	0 / 1	
Herpes zoster			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			

subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine infection			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 185 (0.54%)	2 / 167 (1.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Mycobacterium avium complex infection			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial colitis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory tract infection			
subjects affected / exposed	1 / 185 (0.54%)	2 / 167 (1.20%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	2 / 185 (1.08%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Oesophageal candidiasis			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	4 / 185 (2.16%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (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 / 185 (0.54%)	0 / 167 (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 / 185 (0.00%)	1 / 167 (0.60%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	1 / 185 (0.54%)	0 / 167 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 185 (0.00%)	1 / 167 (0.60%)	
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 + Cabozantinib	Docetaxel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	172 / 185 (92.97%)	147 / 167 (88.02%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	16 / 185 (8.65%)	2 / 167 (1.20%)	
occurrences (all)	22	3	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	17 / 185 (9.19%)	12 / 167 (7.19%)	
occurrences (all)	18	12	
Malaise			
subjects affected / exposed	5 / 185 (2.70%)	9 / 167 (5.39%)	
occurrences (all)	5	9	
Mucosal inflammation			
subjects affected / exposed	11 / 185 (5.95%)	9 / 167 (5.39%)	
occurrences (all)	17	10	
Asthenia			
subjects affected / exposed	42 / 185 (22.70%)	40 / 167 (23.95%)	
occurrences (all)	51	45	
Fatigue			

subjects affected / exposed	41 / 185 (22.16%)	44 / 167 (26.35%)	
occurrences (all)	47	48	
Oedema peripheral			
subjects affected / exposed	6 / 185 (3.24%)	12 / 167 (7.19%)	
occurrences (all)	6	15	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	23 / 185 (12.43%)	25 / 167 (14.97%)	
occurrences (all)	25	25	
Dysphonia			
subjects affected / exposed	15 / 185 (8.11%)	1 / 167 (0.60%)	
occurrences (all)	18	1	
Cough			
subjects affected / exposed	18 / 185 (9.73%)	12 / 167 (7.19%)	
occurrences (all)	20	14	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	16 / 185 (8.65%)	7 / 167 (4.19%)	
occurrences (all)	16	7	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	8 / 185 (4.32%)	12 / 167 (7.19%)	
occurrences (all)	16	19	
Alanine aminotransferase increased			
subjects affected / exposed	36 / 185 (19.46%)	7 / 167 (4.19%)	
occurrences (all)	50	7	
Aspartate aminotransferase increased			
subjects affected / exposed	30 / 185 (16.22%)	4 / 167 (2.40%)	
occurrences (all)	39	4	
Platelet count decreased			
subjects affected / exposed	15 / 185 (8.11%)	0 / 167 (0.00%)	
occurrences (all)	27	0	
Weight decreased			
subjects affected / exposed	27 / 185 (14.59%)	5 / 167 (2.99%)	
occurrences (all)	27	6	
Nervous system disorders			

Dysgeusia			
subjects affected / exposed	20 / 185 (10.81%)	10 / 167 (5.99%)	
occurrences (all)	24	14	
Headache			
subjects affected / exposed	13 / 185 (7.03%)	14 / 167 (8.38%)	
occurrences (all)	14	18	
Dizziness			
subjects affected / exposed	14 / 185 (7.57%)	5 / 167 (2.99%)	
occurrences (all)	15	5	
Neuropathy peripheral			
subjects affected / exposed	4 / 185 (2.16%)	9 / 167 (5.39%)	
occurrences (all)	4	9	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	16 / 185 (8.65%)	1 / 167 (0.60%)	
occurrences (all)	19	1	
Anaemia			
subjects affected / exposed	22 / 185 (11.89%)	37 / 167 (22.16%)	
occurrences (all)	23	46	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	30 / 185 (16.22%)	17 / 167 (10.18%)	
occurrences (all)	33	17	
Nausea			
subjects affected / exposed	44 / 185 (23.78%)	29 / 167 (17.37%)	
occurrences (all)	53	42	
Diarrhoea			
subjects affected / exposed	80 / 185 (43.24%)	38 / 167 (22.75%)	
occurrences (all)	118	62	
Stomatitis			
subjects affected / exposed	28 / 185 (15.14%)	13 / 167 (7.78%)	
occurrences (all)	30	14	
Vomiting			
subjects affected / exposed	27 / 185 (14.59%)	11 / 167 (6.59%)	
occurrences (all)	34	14	
Abdominal pain upper			

subjects affected / exposed	10 / 185 (5.41%)	2 / 167 (1.20%)	
occurrences (all)	11	2	
Abdominal pain			
subjects affected / exposed	21 / 185 (11.35%)	5 / 167 (2.99%)	
occurrences (all)	27	5	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	14 / 185 (7.57%)	6 / 167 (3.59%)	
occurrences (all)	17	7	
Dry skin			
subjects affected / exposed	10 / 185 (5.41%)	7 / 167 (4.19%)	
occurrences (all)	10	7	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	40 / 185 (21.62%)	2 / 167 (1.20%)	
occurrences (all)	53	2	
Alopecia			
subjects affected / exposed	4 / 185 (2.16%)	40 / 167 (23.95%)	
occurrences (all)	4	40	
Rash			
subjects affected / exposed	17 / 185 (9.19%)	13 / 167 (7.78%)	
occurrences (all)	20	14	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	19 / 185 (10.27%)	3 / 167 (1.80%)	
occurrences (all)	24	3	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	26 / 185 (14.05%)	0 / 167 (0.00%)	
occurrences (all)	28	0	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	10 / 185 (5.41%)	19 / 167 (11.38%)	
occurrences (all)	12	23	
Muscle spasms			
subjects affected / exposed	11 / 185 (5.95%)	3 / 167 (1.80%)	
occurrences (all)	12	3	

Arthralgia			
subjects affected / exposed	25 / 185 (13.51%)	19 / 167 (11.38%)	
occurrences (all)	29	22	
Pain in extremity			
subjects affected / exposed	12 / 185 (6.49%)	4 / 167 (2.40%)	
occurrences (all)	14	4	
Back pain			
subjects affected / exposed	17 / 185 (9.19%)	7 / 167 (4.19%)	
occurrences (all)	19	9	
Infections and infestations			
COVID-19			
subjects affected / exposed	12 / 185 (6.49%)	4 / 167 (2.40%)	
occurrences (all)	12	4	
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	18 / 185 (9.73%)	12 / 167 (7.19%)	
occurrences (all)	20	16	
Hypomagnesaemia			
subjects affected / exposed	20 / 185 (10.81%)	4 / 167 (2.40%)	
occurrences (all)	26	5	
Hyponatraemia			
subjects affected / exposed	12 / 185 (6.49%)	10 / 167 (5.99%)	
occurrences (all)	15	10	
Hypokalaemia			
subjects affected / exposed	15 / 185 (8.11%)	8 / 167 (4.79%)	
occurrences (all)	15	9	
Decreased appetite			
subjects affected / exposed	56 / 185 (30.27%)	28 / 167 (16.77%)	
occurrences (all)	62	31	
Hypocalcaemia			
subjects affected / exposed	18 / 185 (9.73%)	7 / 167 (4.19%)	
occurrences (all)	32	7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 March 2023	Protocol GO41892, Version 5: has been amended primarily to update the adverse event management guidelines to align with the recent Atezolizumab Investigator's Brochure, Version 19, and Cabozantinib Investigator’s Brochure, Version 18.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported