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	17 January 2025

Results information

Result version number	v3 (current)
This version publication date	20 November 2025
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	Final
Date of interim/final analysis	17 January 2025
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to evaluate the efficacy of atezolizumab in combination with cabozantinib (Atezo + Cabo) compared with docetaxel monotherapy in participants 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-programmed death ligand 1/programmed cell death protein 1 (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 (ICF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	44 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:

A total of 366 participants with metastatic NSCLC previously treated with anti-PD-L1/PD-1 antibody and platinum-containing chemotherapy took part in the study at 97 investigative sites across 15 countries from 01 October 2020 to 17 January 2025.

Pre-assignment

Screening details:

Participants were randomized in a 1:1 ratio to receive either docetaxel monotherapy or atezolizumab & cabozantinib combination therapy. A total of 14 participants did not receive any study treatment and were therefore excluded from the safety analysis.

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 Monotherapy

Arm description:

Participants received docetaxel, 75 milligrams per square meter (mg/m^2), intravenously (IV) on Day 1 of each 21-day cycle until unacceptable toxicity or disease progression (PD) or loss of clinical benefit as determined by the investigator.

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, 75 mg/m^2, IV on Day 1 of each 21-day cycle.

Arm title	Atezolizumab + Cabozantinib

Arm description:

Participants received atezolizumab, 1200 milligrams (mg), IV, on Day 1 of each 21-day cycle along with cabozantinib, 40 mg, orally, given once a day (QD) on Days 1-21 of each cycle until unacceptable toxicity, PD, or loss of clinical benefit as determined by the investigator.

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, 40 mg, orally, QD, on Days 1-21 of each cycle (Cycle= 21 days)

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:
Atezolizumab, 1200 mg, IV, on Day 1 of each 21-day cycle

Number of subjects in period 1	Docetaxel Monotherapy	Atezolizumab + Cabozantinib
Started	180	186
Safety-evaluable Population	167	185
Completed	0	0
Not completed	180	186
Physician decision	-	1
Death	131	147
Reason Not Specified	-	2
Withdrawal by Subject	29	4
Study Terminated by Sponsor	20	29
Lost to follow-up	-	3

Baseline characteristics

Reporting groups	
Reporting group title	Docetaxel Monotherapy
Reporting group description:	
Participants received docetaxel, 75 milligrams per square meter (mg/m^2), intravenously (IV) on Day 1 of each 21-day cycle until unacceptable toxicity or disease progression (PD) or loss of clinical benefit as determined by the investigator.	
Reporting group title	Atezolizumab + Cabozantinib
Reporting group description:	
Participants received atezolizumab, 1200 milligrams (mg), IV, on Day 1 of each 21-day cycle along with cabozantinib, 40 mg, orally, given once a day (QD) on Days 1-21 of each cycle until unacceptable toxicity, PD, or loss of clinical benefit as determined by the investigator.	

Reporting group values	Docetaxel Monotherapy	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			
Asian	53	41	94
Black or African American	1	2	3
White	111	130	241
Unknown or Not Reported	15	13	28
Ethnicity (NIH/OMB) 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 Monotherapy
Reporting group description:	
Participants received docetaxel, 75 milligrams per square meter (mg/m^2), intravenously (IV) on Day 1 of each 21-day cycle until unacceptable toxicity or disease progression (PD) or loss of clinical benefit as determined by the investigator.	
Reporting group title	Atezolizumab + Cabozantinib
Reporting group description:	
Participants received atezolizumab, 1200 milligrams (mg), IV, on Day 1 of each 21-day cycle along with cabozantinib, 40 mg, orally, given once a day (QD) on Days 1-21 of each cycle until unacceptable toxicity, PD, or loss of clinical benefit as determined by the investigator.	

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS was defined as the time from randomization to death from any cause. 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. Kaplan-Meier method was used to estimate the median. 95% CI for median was computed using the method of Brookmeyer and Crowley. The intent-to-treat (ITT) population included all randomized 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 Monotherapy	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:	
Stratified Analysis	
Comparison groups	Atezolizumab + Cabozantinib v Docetaxel Monotherapy

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

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description:	
Unstratified Analysis	
Comparison groups	Docetaxel Monotherapy 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

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

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

End point description:

PFS=time from randomization to first occurrence of PD, as determined by the investigator per response evaluation criteria in solid tumors version 1.1 (RECIST v1.1), or death from any cause (whichever occurred first). PD= ≥ 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. In addition, sum of diameters also demonstrated an absolute increase of ≥ 5 millimeters (mm). Participants who were alive and did not experience PD at the time of analysis, were censored on the date of last tumor assessment. Participants with no post-baseline tumor assessment were censored at the date of randomization. Kaplan-Meier method was used to estimate the median. 95% CI for median was computed using the method of Brookmeyer and Crowley. ITT population=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 Monotherapy	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: Unstratified Analysis	
Comparison groups	Docetaxel Monotherapy 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

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description: Stratified Analysis	
Comparison groups	Docetaxel Monotherapy 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

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. In addition, any pathological lymph nodes must have a reduction in short axis to < 10 mm. PR= at least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters. 95% CIs for rates were constructed using the Clopper-Pearson method. Percentages have been rounded off. ITT population included all randomized 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 Monotherapy	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 Monotherapy 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 Monotherapy 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: Unstratified Analysis	
Comparison groups	Docetaxel Monotherapy 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: Stratified analysis	
Comparison groups	Docetaxel Monotherapy 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=time from first documented OR to PD, or death, as per investigator per RECIST v1.1 (whichever occurred first). PD=≥ 20% increase in sum of longest diameters (SOLD) of target lesions (TL), taking as reference smallest SOLD of TL recorded since treatment started, including screening/ appearance of new lesions. In addition, sum of diameters (SOD) also demonstrated absolute increase of ≥ 5 mm. Confirmed ORR=percentage of participants with CR/PR on 2 consecutive occasions ≥4 weeks apart, as per investigator per RECIST v1.1. CR=disappearance of all TL. PR=≥ 30% decrease in SOD of all TL. Participants who had not progressed & who did not die at the 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 Brookmeyer & Crowley method. ITT population=participants with confirmed objective response (CR/PR) as per the investigator per RECIST v1.1.

End point type	Secondary

End point timeframe:

Up to approximately 24 months

End point values	Docetaxel Monotherapy	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: 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, performed for patient-reported PF (items 1 to 5) of European Organisation for Research & Treatment of Cancer Quality of Life-Core 30 Questionnaire (EORTC QLQ-C30), was measured on 4-point scale (1=Not at all to 4=Very much). TTCD for PF=time from randomization to first confirmed clinically meaningful decrease (CMD) from baseline in PF score held for ≥2 consecutive assessments/initial CMD (≥10 points) from baseline followed by death from any cause within 21 days or until next tumor assessment, whichever occurs first. Scores were averaged, transformed to 0-100 scale; where higher score represented high/healthy level of functioning. Kaplan-Meier method was used to estimate the median. 95% CI for median was computed using Brookmeyer and Crowley method. ITT population=all randomized participants, whether or not the participant received the assigned treatment. 9999=upper limit of 95% confidence interval (CI) was not estimable due to insufficient events after the median estimate.

End point type	Secondary

End point timeframe:

Up to approximately 24 months

End point values	Docetaxel Monotherapy	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: Stratified Analysis	
Comparison groups	Docetaxel Monotherapy v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority[5]
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:

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

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description: Unstratified Analysis	
Comparison groups	Docetaxel Monotherapy 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

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 PD as assessed by the investigator according to RECIST v1.1 at 6 months and 1 year after randomization. PD was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum of diameters at prior timepoints, including baseline. In addition, the sum of diameters also demonstrated an absolute increase of ≥ 5 mm. Kaplan-Meier method was used to estimate the median. 95% CI for median was computed using the method of Brookmeyer and Crowley. Percentages have been rounded off. ITT population included all randomized participants, whether or not the participant received the assigned treatment.

End point type	Secondary

End point timeframe:

6 months and 1 year

End point values	Docetaxel Monotherapy	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 1 year

Comparison groups	Docetaxel Monotherapy 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

Statistical analysis title	Docetaxel, Atezolizumab + Cabozantinib
Statistical analysis description:	
At 6 months	
Comparison groups	Docetaxel Monotherapy 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

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

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

End point description:

TTCD, performed for GHS and quality of life (QoL) (items 29 and 30) of EORTC QLQ-C30, was measured on 7-point scale (very poor to excellent). TTCD for GHS/QoL=time from randomization to first confirmed CMD from baseline in GHS/QoL score held for ≥2 consecutive assessments/initial CMD (≥10 points) from baseline followed by death from any cause within 21 days or until next tumor assessment, whichever occurs first. Scores were averaged, transformed to 0-100 scale; where higher score represented better health-related QoL. Kaplan-Meier method was used to estimate the median. 95% CI for median was computed using Brookmeyer and Crowley method. ITT population=all randomized participants, whether or not the participant received the assigned treatment. 9999=upper limit of 95% CI was not estimable due to insufficient events after the median estimate.

End point type	Secondary

End point timeframe:

Up to approximately 24 months

End point values	Docetaxel Monotherapy	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 Monotherapy 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 Monotherapy v Atezolizumab + Cabozantinib
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	superiority[6]
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:

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

Secondary: OS Rates

End point title	OS Rates

End point description:

OS rates were defined as the percentage of participants who were alive at 1 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. Kaplan-Meier method was used to estimate the median. 95% CI for median was computed using the method of Brookmeyer and Crowley. Percentages have been rounded off. ITT population is defined as all randomized participants, whether or not the participant received the assigned treatment. 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. 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. 99999=survival rate at the 2-year time point was not estimable as there were no participants with 24 months or more of survival follow-up.

End point type	Secondary

End point timeframe:

1 and 2 years

End point values	Docetaxel Monotherapy	Atezolizumab + Cabozantinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	186		
Units: percentage of participants				
number (confidence interval 95%)				
1 year	44.12 (36.20 to 52.05)	43.27 (35.97 to 50.57)		
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 Monotherapy 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: Percentage of Participants With Adverse Events (AEs)

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

End point description:

An AE was defined as any untoward medical occurrence in a clinical investigation patient administered a pharmaceutical product, regardless of causal attribution. An AE can therefore be any of the following: unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product; any new disease or exacerbation of an existing disease; recurrence of an intermittent medical condition not present at baseline; any deterioration in a laboratory value or other clinical test; AEs related to a protocol-mandated intervention. AEs were assessed using National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0 (NCI CTCAE, v5.0). Percentages have been rounded off. Safety-evaluable population=all randomized participants who had received any amount of study drug, with participants grouped according to the actual treatment received.

End point type	Secondary

End point timeframe:

Up to approximately 41.4 months

End point values	Docetaxel Monotherapy	Atezolizumab + Cabozantinib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	167	185		
Units: percentage of participants				
number (not applicable)	94.0	98.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Serum Concentration (Cmin) of Atezolizumab

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

End point description:

Pharmacokinetic (PK)-evaluable population for atezolizumab included all participants who had received any dose of atezolizumab and who had evaluable PK samples. Number analyzed is the number of participants with data available for analysis at the specified timepoint. Different participants may have contributed data for each timepoint. 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 (Cycle=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: No statistical analysis for this end point.

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: Maximum Serum Concentration (Cmax) of Atezolizumab

End point title	Maximum Serum Concentration (Cmax) of Atezolizumab[8]

End point description:

PK-evaluable population included all participants who had received any dose of atezolizumab and who had evaluable PK samples.

End point type	Secondary

End point timeframe:

30 min postdose on Day 1 of Cycle 1 (Cycle=21 days)

Notes:

[8] - 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: No statistical analysis for this end point.

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: Minimum Plasma Concentration (Cmin) of Cabozantinib

End point title	Minimum Plasma Concentration (Cmin) of Cabozantinib[9]

End point description:

PK-evaluable population included all participants who had received any dose of cabozantinib and who had evaluable PK samples. n=number of participants with data available for analysis at the specified timepoint. Different participants may have contributed data for each timepoint. 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:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

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) Cycle 2 Day 1 (n=163)	9999 (± 9999) 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[10]

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:

[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: No statistical analysis for this end point.

End point values	Atezolizumab + Cabozantinib			
Subject group type	Reporting group			
Number of subjects analysed	0[11]			
Units: µg/ml				
geometric mean (geometric coefficient of variation)	()			

Notes:

[11] - 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: Number of Participants with Anti-Drug Antibodies (ADAs) to Atezolizumab

End point title	Number of Participants with Anti-Drug Antibodies (ADAs) to Atezolizumab[12]

End point description:

Participants were considered to be ADA positive if they were ADA negative or had missing data at baseline but developed an ADA response following study drug exposure (treatment-induced ADA response), or if they were ADA positive at baseline and the titer of one or more post-baseline samples was at least 0.60 titer unit greater than the titer of the baseline sample (treatment-enhanced ADA response). The total number of participants who developed ADAs to atezolizumab was determined by summing the ADA-positive participants across all timepoints. Safety-evaluable population included all randomized participants who had received any amount of study drug, with participants grouped

according to the actual treatment received. Number analyzed 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:

[12] - 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: No statistical analysis for this end point.

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:

All-cause mortality: Up to 44.6 months
SAE and other AEs: Up to 41.4 months

Adverse event reporting additional description:

Safety-evaluable population included all randomized participants who had received any amount of study drug. A total of 14 participants did not receive any study treatment and were therefore excluded from the safety analysis.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	Atezolizumab + Cabozantinib

Reporting group description:

Participants received atezolizumab, 1200 mg, IV, on Day 1 of each 21-day cycle along with cabozantinib, 40 mg, orally, given QD on Days 1-21 of each cycle until unacceptable toxicity, PD, or loss of clinical benefit as determined by the investigator.

Reporting group title	Docetaxel Monotherapy

Reporting group description:

Participants received docetaxel, 75 mg/m^2, IV on Day 1 of each 21-day cycle until unacceptable toxicity or PD or loss of clinical benefit as determined by the investigator.

Serious adverse events	Atezolizumab + Cabozantinib	Docetaxel Monotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	76 / 185 (41.08%)	58 / 167 (34.73%)	
number of deaths (all causes)	149	130	
number of deaths resulting from adverse events	4	1	
Vascular disorders			
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	
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	
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			
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	
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	
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	
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	
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	
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	
Immune system disorders			
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	
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	
Respiratory, thoracic and mediastinal disorders			
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	
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	
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	
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	
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	
Pleural effusion			
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	
Psychiatric disorders			
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	
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	
Investigations			
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	
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	
Lipase increased			

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			
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	
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	
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	
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	
Atrial fibrillation			
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 / 1	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	

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	
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	
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	
Nervous system disorders			
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	
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	
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	
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	
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	
Blood and lymphatic system disorders			
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	
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	
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	
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	
Gastrointestinal disorders			
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	
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 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	
Diarrhoea			

subjects affected / exposed	4 / 185 (2.16%)	3 / 167 (1.80%)	
occurrences causally related to treatment / all	2 / 4	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	
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			
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	
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	
Renal and urinary disorders			
Acute kidney injury			
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	
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	

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	
Adrenal insufficiency			
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			
Spinal osteoarthritis			
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	
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	
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	
Infections and infestations			
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	
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	
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	
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	2 / 185 (1.08%)	2 / 167 (1.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
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	
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	
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	
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	
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	
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	
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	
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	
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	
Anal abscess			
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 necrotising			
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	
Metabolism and nutrition disorders			
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	
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	
Cachexia			

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	

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

Non-serious adverse events	Atezolizumab + Cabozantinib	Docetaxel Monotherapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	173 / 185 (93.51%)	148 / 167 (88.62%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	17 / 185 (9.19%)	2 / 167 (1.20%)	
occurrences (all)	25	3	
General disorders and administration site conditions			
Mucosal inflammation			
subjects affected / exposed	11 / 185 (5.95%)	9 / 167 (5.39%)	
occurrences (all)	17	10	
Asthenia			
subjects affected / exposed	43 / 185 (23.24%)	40 / 167 (23.95%)	
occurrences (all)	53	45	
Malaise			
subjects affected / exposed	5 / 185 (2.70%)	9 / 167 (5.39%)	
occurrences (all)	5	9	
Fatigue			
subjects affected / exposed	42 / 185 (22.70%)	44 / 167 (26.35%)	
occurrences (all)	48	48	
Pyrexia			
subjects affected / exposed	20 / 185 (10.81%)	12 / 167 (7.19%)	
occurrences (all)	21	12	
Oedema peripheral			
subjects affected / exposed	8 / 185 (4.32%)	12 / 167 (7.19%)	
occurrences (all)	8	15	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	27 / 185 (14.59%)	25 / 167 (14.97%)	
occurrences (all)	29	25	
Dysphonia			
subjects affected / exposed	16 / 185 (8.65%)	1 / 167 (0.60%)	
occurrences (all)	19	1	
Cough			
subjects affected / exposed	20 / 185 (10.81%)	12 / 167 (7.19%)	
occurrences (all)	25	14	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	17 / 185 (9.19%)	7 / 167 (4.19%)	
occurrences (all)	18	7	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	36 / 185 (19.46%)	7 / 167 (4.19%)	
occurrences (all)	53	7	
Aspartate aminotransferase increased			
subjects affected / exposed	31 / 185 (16.76%)	4 / 167 (2.40%)	
occurrences (all)	42	4	
Platelet count decreased			
subjects affected / exposed	15 / 185 (8.11%)	0 / 167 (0.00%)	
occurrences (all)	27	0	
Weight decreased			
subjects affected / exposed	30 / 185 (16.22%)	6 / 167 (3.59%)	
occurrences (all)	30	7	
Neutrophil count decreased			
subjects affected / exposed	8 / 185 (4.32%)	12 / 167 (7.19%)	
occurrences (all)	17	19	
Amylase increased			
subjects affected / exposed	10 / 185 (5.41%)	2 / 167 (1.20%)	
occurrences (all)	11	2	
Nervous system disorders			
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	
Dysgeusia			
subjects affected / exposed	20 / 185 (10.81%)	10 / 167 (5.99%)	
occurrences (all)	24	14	
Headache			
subjects affected / exposed	14 / 185 (7.57%)	14 / 167 (8.38%)	
occurrences (all)	16	18	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	24 / 185 (12.97%)	38 / 167 (22.75%)	
occurrences (all)	26	47	
Thrombocytopenia			
subjects affected / exposed	17 / 185 (9.19%)	1 / 167 (0.60%)	
occurrences (all)	20	1	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	31 / 185 (16.76%)	17 / 167 (10.18%)	
occurrences (all)	35	17	
Nausea			
subjects affected / exposed	47 / 185 (25.41%)	29 / 167 (17.37%)	
occurrences (all)	56	42	
Diarrhoea			
subjects affected / exposed	83 / 185 (44.86%)	38 / 167 (22.75%)	
occurrences (all)	134	62	
Abdominal pain			
subjects affected / exposed	21 / 185 (11.35%)	5 / 167 (2.99%)	
occurrences (all)	27	5	
Abdominal pain upper			
subjects affected / exposed	11 / 185 (5.95%)	2 / 167 (1.20%)	
occurrences (all)	12	2	
Vomiting			
subjects affected / exposed	29 / 185 (15.68%)	11 / 167 (6.59%)	
occurrences (all)	36	14	
Stomatitis			

subjects affected / exposed	28 / 185 (15.14%)	13 / 167 (7.78%)	
occurrences (all)	30	14	
Skin and subcutaneous tissue disorders			
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	
Pruritus			
subjects affected / exposed	15 / 185 (8.11%)	6 / 167 (3.59%)	
occurrences (all)	19	7	
Dry skin			
subjects affected / exposed	11 / 185 (5.95%)	7 / 167 (4.19%)	
occurrences (all)	11	7	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	40 / 185 (21.62%)	2 / 167 (1.20%)	
occurrences (all)	54	2	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	22 / 185 (11.89%)	3 / 167 (1.80%)	
occurrences (all)	30	3	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	30 / 185 (16.22%)	0 / 167 (0.00%)	
occurrences (all)	32	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	26 / 185 (14.05%)	20 / 167 (11.98%)	
occurrences (all)	31	23	
Pain in extremity			
subjects affected / exposed	12 / 185 (6.49%)	4 / 167 (2.40%)	
occurrences (all)	15	4	
Back pain			
subjects affected / exposed	18 / 185 (9.73%)	7 / 167 (4.19%)	
occurrences (all)	20	9	

Myalgia			
subjects affected / exposed	11 / 185 (5.95%)	19 / 167 (11.38%)	
occurrences (all)	14	23	
Muscle spasms			
subjects affected / exposed	11 / 185 (5.95%)	3 / 167 (1.80%)	
occurrences (all)	13	3	
Infections and infestations			
COVID-19			
subjects affected / exposed	14 / 185 (7.57%)	4 / 167 (2.40%)	
occurrences (all)	15	4	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	12 / 185 (6.49%)	10 / 167 (5.99%)	
occurrences (all)	17	10	
Hypomagnesaemia			
subjects affected / exposed	23 / 185 (12.43%)	4 / 167 (2.40%)	
occurrences (all)	29	5	
Hypoalbuminaemia			
subjects affected / exposed	20 / 185 (10.81%)	12 / 167 (7.19%)	
occurrences (all)	23	16	
Hypocalcaemia			
subjects affected / exposed	20 / 185 (10.81%)	7 / 167 (4.19%)	
occurrences (all)	35	7	
Decreased appetite			
subjects affected / exposed	59 / 185 (31.89%)	28 / 167 (16.77%)	
occurrences (all)	64	31	
Hypokalaemia			
subjects affected / exposed	15 / 185 (8.11%)	8 / 167 (4.79%)	
occurrences (all)	15	9	
Hypophosphataemia			
subjects affected / exposed	12 / 185 (6.49%)	5 / 167 (2.99%)	
occurrences (all)	13	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2020	- Exclusion criteria were added for severe hepatic impairment and known allergy or hypersensitivity to the cabozantinib formulation.
18 March 2021	- The exclusion criteria were amended to exclude participants with known repressor of silencing 1 (ROS1) rearrangements, or BRAF valine (V) substituted by glutamic acid (E) at amino acid 600 (BRAF V600E) mutations, or other actionable oncogenes with approved therapies if available; to clarify the timeline for prior ischemic events or significant cardiovascular disease; to clarify mineralocorticoid or corticosteroid use. -The use of direct acting oral anticoagulants was clarified in the exclusion criteria, permitted therapy, and management of thromboembolic events associated with cabozantinib. -The exclusion criteria were amended to exclude participants with arterial dissection and other significant vascular disease in order to align with cabozantinib Summary of Product Characteristics (SmPC) -Stratification factors for randomization were clarified to require PD before using a second-line agent, and to distinguish between platinum-containing chemotherapy given without anti-PD-L1/PD-1 antibody versus platinum-containing chemotherapy given in combination with anti-PD-L1/PD-1 antibody.
10 March 2022	- A benefit-risk assessment and guidance on concomitant administration of COVID-19 vaccines with atezolizumab were added. - Immune RECIST (iRECIST) appendix was removed to align with a program level decision to no longer perform exploratory analyses of response rate and progression-free survival according to iRECIST criteria.
22 March 2023	- Two newly approved indications for cabozantinib were added to align with the cabozantinib investigator's brochure, version 18. - The completion of patient-reported outcome (PRO) questionnaires was no longer required after the final OS analysis. - The duration of follow-up after the completion of final OS analysis was specified as 6 months after patient's last dose of study treatment. - The end-of-study definition was updated to include the additional criteria of when the last data point required for safety follow-up has been received (if it occurs later than the required number of deaths for the final analysis OS), and the last patient's last visit (LPLV) has occurred. Participants may continue study treatment until the development of PD, unacceptable toxicity, patient consent withdrawal, or sponsor's decision to terminate the study, whichever occurs first. The Sponsor will provide a written notification to investigators if the study has terminated and the investigators, in consultation with the medical monitor, may offer suitable participants with potential enrollment to the continued access program or another study for continued access to study treatment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported