



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 | v1 |
| This version publication date | 14 October 2023 |
| First version publication date | 14 October 2023 |

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/m² 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: 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 \geq 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 ^[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

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: | |
| 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 | = 0.2408 |
| 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

| | |
|-----------------------------------|---|
| 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 |

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. Number analysed is the number of participants with data available for analysis at the specified timepoints. | |
| 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 (n=36,72) | 23.66 (16.98 to 30.33) | 39.51 (32.42 to 46.59) | | |
| At 1 year (n=10,21) | 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 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 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: OS Rates | |
| End point title | OS Rates |
| End point description: | |
| <p>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. ITT population is defined as all randomised participants, whether or not the participant received the assigned treatment. Number analysed is the number of participants with data available for analysis at the specified timepoints. Here 99999 indicates participants were not analysed for this endpoint at the given timepoint. By the time the OS at 2 years was analyzed, the participants had either died or were censored prior to 24 months. Therefore, there were no participants available for analyses at the 2-year timepoint.</p> | |
| 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 (n=54,65) | 44.12 (36.20 to 52.05) | 43.27 (35.97 to 50.57) | | |
| At 2 years (n=0,0) | 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: 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 ^[7] | 0 ^[8] | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |

Notes:

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

[8] - 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 Serum Concentration (Cmin) of Atezolizumab

| | |
|-----------------|---|
| End point title | Minimum Serum Concentration (Cmin) of Atezolizumab ^[9] |
|-----------------|---|

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:

[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: Pharmacokinetics was analyzed for Atezolizumab only 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: Maximum Serum Concentration (Cmax) of Atezolizumab

| | |
|-----------------|--|
| End point title | Maximum Serum Concentration (Cmax) of Atezolizumab ^[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.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

30 min Post-dose on Day 1 of Cycle 1 (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 Atezolizumab 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) | 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 ^[11] |
|-----------------|---|

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:

[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: 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 ^[12] |
|-----------------|---|

End point description:

PK of Cabozantinib was well characterized through the cabozantinib development for mono-therapy. Therefore, there was no need to measure Cmax 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:

[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: Pharmacokinetics was analyzed for Cabozantinib only for this endpoint. 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 ^[13] | | | |
| Units: µg/ml | | | | |
| geometric mean (geometric coefficient of variation) | () | | | |

Notes:

[13] - 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 ^[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.

| | |
|-----------------|------------|
| 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/m² 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 | 105 | |
| 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 | | | |

| | | | |
|---|-----------------|-----------------|--|
| 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 | |
| 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 | |
| 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 | | | |
| 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 | | | |
| 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 | |
| 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 | |
| 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 | |
| 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 | | | |
| 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 | |

| | | | |
|---|-----------------|-----------------|--|
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| Nervous system disorders | | | |

| | | | |
|---|-----------------|-----------------|--|
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| Gastrointestinal disorders | | | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 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 | |
| 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 | |
| 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 | | | |
| 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 | |
| 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 | |
| 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 | | | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |
| 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 | |

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 | | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 6 / 185 (3.24%) | 12 / 167 (7.19%) | |
| occurrences (all) | 6 | 15 | |
| Fatigue | | | |
| subjects affected / exposed | 41 / 185 (22.16%) | 44 / 167 (26.35%) | |
| occurrences (all) | 47 | 48 | |
| 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 occurrences (all) | 42 / 185 (22.70%) 51 | 40 / 167 (23.95%) 45 | |
| Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Dysphonia subjects affected / exposed occurrences (all) | 23 / 185 (12.43%) 25 18 / 185 (9.73%) 20 15 / 185 (8.11%) 18 | 25 / 167 (14.97%) 25 12 / 167 (7.19%) 14 1 / 167 (0.60%) 1 | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) | 16 / 185 (8.65%) 16 | 7 / 167 (4.19%) 7 | |
| Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all) Platelet count decreased subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all) Neutrophil count decreased subjects affected / exposed occurrences (all) | 36 / 185 (19.46%) 50 30 / 185 (16.22%) 39 15 / 185 (8.11%) 27 27 / 185 (14.59%) 27 8 / 185 (4.32%) 16 | 7 / 167 (4.19%) 7 4 / 167 (2.40%) 4 0 / 167 (0.00%) 0 5 / 167 (2.99%) 6 12 / 167 (7.19%) 19 | |
| Nervous system disorders Neuropathy peripheral subjects affected / exposed occurrences (all) | 4 / 185 (2.16%) 4 | 9 / 167 (5.39%) 9 | |

| | | | |
|---|--------------------------|-------------------------|--|
| Dysgeusia subjects affected / exposed occurrences (all) | 20 / 185 (10.81%) 24 | 10 / 167 (5.99%) 14 | |
| Headache subjects affected / exposed occurrences (all) | 13 / 185 (7.03%) 14 | 14 / 167 (8.38%) 18 | |
| Dizziness subjects affected / exposed occurrences (all) | 14 / 185 (7.57%) 15 | 5 / 167 (2.99%) 5 | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) | 22 / 185 (11.89%) 23 | 37 / 167 (22.16%) 46 | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 16 / 185 (8.65%) 19 | 1 / 167 (0.60%) 1 | |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) | 30 / 185 (16.22%) 33 | 17 / 167 (10.18%) 17 | |
| Nausea subjects affected / exposed occurrences (all) | 44 / 185 (23.78%) 53 | 29 / 167 (17.37%) 42 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 80 / 185 (43.24%) 118 | 38 / 167 (22.75%) 62 | |
| Abdominal pain subjects affected / exposed occurrences (all) | 21 / 185 (11.35%) 27 | 5 / 167 (2.99%) 5 | |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 10 / 185 (5.41%) 11 | 2 / 167 (1.20%) 2 | |
| Vomiting subjects affected / exposed occurrences (all) | 27 / 185 (14.59%) 34 | 11 / 167 (6.59%) 14 | |
| Stomatitis | | | |

| | | | |
|--|-------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 28 / 185 (15.14%) 30 | 13 / 167 (7.78%) 14 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 17 / 185 (9.19%) | 13 / 167 (7.78%) | |
| occurrences (all) | 20 | 14 | |
| Alopecia | | | |
| subjects affected / exposed | 4 / 185 (2.16%) | 40 / 167 (23.95%) | |
| occurrences (all) | 4 | 40 | |
| 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 erythrodysesthesia syndrome | | | |
| subjects affected / exposed | 40 / 185 (21.62%) | 2 / 167 (1.20%) | |
| occurrences (all) | 53 | 2 | |
| 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 | |
| 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 occurrences (all) | 17 / 185 (9.19%) 19 | 7 / 167 (4.19%) 9 | |
| Muscle spasms subjects affected / exposed occurrences (all) | 11 / 185 (5.95%) 12 | 3 / 167 (1.80%) 3 | |
| Infections and infestations COVID-19 subjects affected / exposed occurrences (all) | 12 / 185 (6.49%) 12 | 4 / 167 (2.40%) 4 | |
| Metabolism and nutrition disorders Hypocalcaemia subjects affected / exposed occurrences (all) | 18 / 185 (9.73%) 32 | 7 / 167 (4.19%) 7 | |
| Decreased appetite subjects affected / exposed occurrences (all) | 56 / 185 (30.27%) 62 | 28 / 167 (16.77%) 31 | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 15 / 185 (8.11%) 15 | 8 / 167 (4.79%) 9 | |
| Hyponatraemia subjects affected / exposed occurrences (all) | 12 / 185 (6.49%) 15 | 10 / 167 (5.99%) 10 | |
| Hypomagnesaemia subjects affected / exposed occurrences (all) | 20 / 185 (10.81%) 26 | 4 / 167 (2.40%) 5 | |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 18 / 185 (9.73%) 20 | 12 / 167 (7.19%) 16 | |

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