



Clinical trial results:

A Phase I/III, Randomized, Double-Blind, Placebo-Controlled Study of Carboplatin Plus Etoposide With or Without Atezolizumab (Anti-PD-L1 Antibody) in Patients With Untreated Extensive-Stage Small Cell Lung Cancer

Summary

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2015-004861-97 |
| Trial protocol | DE PL HU CZ GB AT GR ES FR IT |
| Global end of trial date | 07 July 2022 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v3 (current) |
| This version publication date | 06 July 2023 |
| First version publication date | 05 May 2019 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | GO30081 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02763579 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 07 July 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|--------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 07 July 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This randomized, Phase I/III, multicenter, double-blinded, placebo-controlled study was designed to evaluate the safety and efficacy of atezolizumab (anti-programmed death-ligand 1 [PD-L1] antibody) in combination with carboplatin plus (+) etoposide compared with treatment with placebo + carboplatin + etoposide in subjects with chemotherapy-naïve extensive-stage small cell lung cancer.

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 | 07 June 2016 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy, Ethical reason |
| Long term follow-up duration | 32 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Australia: 11 |
| Country: Number of subjects enrolled | China: 100 |
| Country: Number of subjects enrolled | Japan: 42 |
| Country: Number of subjects enrolled | Korea, Republic of: 17 |
| Country: Number of subjects enrolled | Taiwan: 10 |
| Country: Number of subjects enrolled | Austria: 20 |
| Country: Number of subjects enrolled | Czechia: 17 |
| Country: Number of subjects enrolled | Germany: 9 |
| Country: Number of subjects enrolled | Spain: 25 |
| Country: Number of subjects enrolled | France: 7 |
| Country: Number of subjects enrolled | United Kingdom: 10 |
| Country: Number of subjects enrolled | Mexico: 4 |
| Country: Number of subjects enrolled | United States: 86 |
| Country: Number of subjects enrolled | Brazil: 4 |
| Country: Number of subjects enrolled | Chile: 6 |
| Country: Number of subjects enrolled | Greece: 11 |
| Country: Number of subjects enrolled | Hungary: 19 |
| Country: Number of subjects enrolled | Italy: 15 |

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Poland: 45 |
| Country: Number of subjects enrolled | Russian Federation: 30 |
| Country: Number of subjects enrolled | Serbia: 15 |
| Worldwide total number of subjects | 503 |
| EEA total number of subjects | 168 |

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) | 286 |
| From 65 to 84 years | 215 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 114 centers in 21 countries: United States of America, Poland, Japan, Russia, Spain, Austria, Hungary, Czech Republic, South Korea, Italy, Serbia, Australia, Greece, United Kingdom, Germany, Taiwan, France, Chile, Brazil, Mexico, and China.

Pre-assignment

Screening details:

Total study population included 503 participants. Global population included 403 participants. An additional 100 participants enrolled during the China Extension. Total China population included 10 Chinese participants from Global population plus 100 participants from the China extension.

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | No |
| Arm title | Placebo + Carboplatin + Etoposide - Global |

Arm description:

Participants in the Global population received intravenous infusions of placebo in combination with carboplatin to achieve an initial target AUC of 5 mg/mL/min followed by etoposide 100 mg/m² on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m² was administered alone. Thereafter, participants received maintenance (Cycle 5 onward) placebo on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Placebo intravenous infusion was administered on Day 1 of each 21-day cycle during the induction phase (Cycles 1-4) and maintenance phase (Cycle 5 onward).

| | |
|--|-----------------|
| Investigational medicinal product name | Etoposide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Etoposide intravenous infusion was administered at a dose of 100 mg/m² on Days 1, 2, and 3 of each 21-day cycle during the induction phase (Cycles 1-4).

| | |
|--|-----------------|
| Investigational medicinal product name | Carboplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Carboplatin intravenous infusion to achieve an initial target AUC of 5 mg/mL/min was administered on Day 1 of each 21-day cycle during the induction phase (Cycles 1-4).

| | |
|------------------|---|
| Arm title | Atezolizumab + Carboplatin + Etoposide - Global |
|------------------|---|

Arm description:

Participants in the Global population received intravenous infusions of atezolizumab 1200 milligrams (mg) in combination with carboplatin to achieve an initial target area under the concentration-time curve (AUC) of 5 milligrams per milliliter per minute (mg/mL/min) followed by etoposide 100 milligrams per square meter (mg/m²) on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m² was administered alone. Thereafter, participants received maintenance (Cycle 5 onward) atezolizumab 1200 mg on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Atezolizumab |
| Investigational medicinal product code | |
| Other name | MPDL3280A, RO5541267, Tecentriq |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Atezolizumab intravenous infusion was administered at a dose of 1200 mg on Day 1 of each 21-day cycle during the induction phase (Cycles 1-4) and maintenance phase (Cycle 5 onward).

| | |
|--|-----------------|
| Investigational medicinal product name | Etoposide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Etoposide intravenous infusion was administered at a dose of 100 mg/m² on Days 1, 2, and 3 of each 21-day cycle during the induction phase (Cycles 1-4).

| | |
|--|-----------------|
| Investigational medicinal product name | Carboplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Carboplatin intravenous infusion to achieve an initial target AUC of 5 mg/mL/min was administered on Day 1 of each 21-day cycle during the induction phase (Cycles 1-4).

| | |
|------------------|---|
| Arm title | Placebo + Carboplatin + Etoposide - China |
|------------------|---|

Arm description:

Participants in the China population received intravenous infusions of placebo in combination with carboplatin to achieve an initial target AUC of 5 mg/mL/min followed by etoposide 100 mg/m² on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m² was administered alone. Thereafter, participants received maintenance (Cycle 5 onward) placebo on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:
Placebo intravenous infusion was administered on Day 1 of each 21-day cycle during the induction phase (Cycles 1-4) and maintenance phase (Cycle 5 onward).

| | |
|--|-----------------|
| Investigational medicinal product name | Etoposide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:
Etoposide intravenous infusion was administered at a dose of 100 mg/m² on Days 1, 2, and 3 of each 21-day cycle during the induction phase (Cycles 1-4).

| | |
|--|-----------------|
| Investigational medicinal product name | Carboplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:
Carboplatin intravenous infusion to achieve an initial target AUC of 5 mg/mL/min was administered on Day 1 of each 21-day cycle during the induction phase (Cycles 1-4).

| | |
|------------------|--|
| Arm title | Atezolizumab + Carboplatin + Etoposide - China |
|------------------|--|

Arm description:

Participants in the China population received intravenous infusions of atezolizumab 1200 milligrams (mg) in combination with carboplatin to achieve an initial target area under the concentration-time curve (AUC) of 5 milligrams per milliliter per minute (mg/mL/min) followed by etoposide 100 milligrams per square meter (mg/m²) on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m² was administered alone. Thereafter, participants received maintenance (Cycle 5 onward) atezolizumab 1200 mg on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

| | |
|--|---------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Atezolizumab |
| Investigational medicinal product code | |
| Other name | MPDL3280A, RO5541267, Tecentriq |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:
Atezolizumab intravenous infusion was administered at a dose of 1200 mg on Day 1 of each 21-day cycle during the induction phase (Cycles 1-4) and maintenance phase (Cycle 5 onward).

| | |
|--|-----------------|
| Investigational medicinal product name | Etoposide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:
Etoposide intravenous infusion was administered at a dose of 100 mg/m² on Days 1, 2, and 3 of each 21-day cycle during the induction phase (Cycles 1-4).

| | |
|--|-----------------|
| Investigational medicinal product name | Carboplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:
Carboplatin intravenous infusion to achieve an initial target AUC of 5 mg/mL/min was administered on Day 1 of each 21-day cycle during the induction phase (Cycles 1-4).

| Number of subjects in period 1 | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - Global | Placebo + Carboplatin + Etoposide - China |
|---------------------------------------|--|---|---|
| Started | 202 | 201 | 53 |
| Completed | 0 | 0 | 0 |
| Not completed | 202 | 201 | 53 |
| Consent withdrawn by subject | 12 | 18 | 3 |
| Physician decision | - | 2 | - |
| Study Terminated By Sponsor | 21 | 26 | 3 |
| Death | 167 | 151 | 46 |
| Lost to follow-up | 2 | 4 | 1 |

| Number of subjects in period 1 | Atezolizumab + Carboplatin + Etoposide - China |
|---------------------------------------|--|
| Started | 57 |
| Completed | 0 |
| Not completed | 57 |
| Consent withdrawn by subject | 3 |
| Physician decision | 1 |
| Study Terminated By Sponsor | 4 |
| Death | 48 |
| Lost to follow-up | 1 |

Baseline characteristics

Reporting groups

| Reporting group title | Overall Period |
|---|----------------|
| Reporting group description: | |
| The total study population included 503 participants. The Global population included 403 participants. An additional 100 participants enrolled during the China Extension. The total China population included 10 Chinese participants from the Global population plus 100 participants from the China extension. 10 participants were part of the Global as well as China populations. | |

| Reporting group values | Overall Period | Total | |
|---|----------------|-------|--|
| Number of subjects | 503 | 503 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 286 | 286 | |
| From 65-84 years | 215 | 215 | |
| 85 years and over | 2 | 2 | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 63.0 | | |
| standard deviation | ± 8.9 | - | |
| Sex: Female, Male | | | |
| As reported from Electronic Case Report Form (eCRF). | | | |
| Units: Participants | | | |
| Female | 164 | 164 | |
| Male | 339 | 339 | |

End points

End points reporting groups

| | |
|-----------------------|--|
| Reporting group title | Placebo + Carboplatin + Etoposide - Global |
|-----------------------|--|

Reporting group description:

Participants in the Global population received intravenous infusions of placebo in combination with carboplatin to achieve an initial target AUC of 5 mg/mL/min followed by etoposide 100 mg/m² on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m² was administered alone. Thereafter, participants received maintenance (Cycle 5 onward) placebo on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

| | |
|-----------------------|---|
| Reporting group title | Atezolizumab + Carboplatin + Etoposide - Global |
|-----------------------|---|

Reporting group description:

Participants in the Global population received intravenous infusions of atezolizumab 1200 milligrams (mg) in combination with carboplatin to achieve an initial target area under the concentration-time curve (AUC) of 5 milligrams per milliliter per minute (mg/mL/min) followed by etoposide 100 milligrams per square meter (mg/m²) on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m² was administered alone. Thereafter, participants received maintenance (Cycle 5 onward) atezolizumab 1200 mg on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

| | |
|-----------------------|---|
| Reporting group title | Placebo + Carboplatin + Etoposide - China |
|-----------------------|---|

Reporting group description:

Participants in the China population received intravenous infusions of placebo in combination with carboplatin to achieve an initial target AUC of 5 mg/mL/min followed by etoposide 100 mg/m² on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m² was administered alone. Thereafter, participants received maintenance (Cycle 5 onward) placebo on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

| | |
|-----------------------|--|
| Reporting group title | Atezolizumab + Carboplatin + Etoposide - China |
|-----------------------|--|

Reporting group description:

Participants in the China population received intravenous infusions of atezolizumab 1200 milligrams (mg) in combination with carboplatin to achieve an initial target area under the concentration-time curve (AUC) of 5 milligrams per milliliter per minute (mg/mL/min) followed by etoposide 100 milligrams per square meter (mg/m²) on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m² was administered alone. Thereafter, participants received maintenance (Cycle 5 onward) atezolizumab 1200 mg on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

Primary: Duration of Progression-Free Survival (PFS) as Assessed by the Investigator Using RECIST v1.1 in the Global Population

| | |
|-----------------|---|
| End point title | Duration of Progression-Free Survival (PFS) as Assessed by the Investigator Using RECIST v1.1 in the Global Population ^[1] |
|-----------------|---|

End point description:

Progression is defined using Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.0), as at least 20% increase in the sum of the longest diameter of target lesions compared to baseline, or unequivocal progression in non-target lesion(s), or the appearance of new lesion(s).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline until PD or death, whichever occurs first (up to approximately 23 months)

Notes:

[1] - 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 the endpoint.

| End point values | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - Global | | |
|----------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 202 | 201 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 4.3 (4.2 to 4.5) | 5.2 (4.4 to 5.6) | | |

Statistical analyses

| Statistical analysis title | PFS Statistical Analysis |
|---|--|
| Comparison groups | Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global |
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.017 |
| Method | Logrank |
| Parameter estimate | Stratified Hazard Ratio |
| Point estimate | 0.77 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.62 |
| upper limit | 0.96 |

Primary: Duration of Overall Survival (OS) in the Global Population

| | |
|------------------------|---|
| End point title | Duration of Overall Survival (OS) in the Global Population ^[2] |
| End point description: | OS is defined as the time from randomization to death from any cause. |
| End point type | Primary |
| End point timeframe: | Baseline until death from any cause (up to approximately 23 months) |

Notes:

[2] - 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 the endpoint.

| End point values | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - Global | | |
|----------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 202 | 201 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 10.3 (9.3 to 11.3) | 12.3 (10.8 to 15.9) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | OS Statistical Analysis |
| Comparison groups | Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global |
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0069 |
| Method | Logrank |
| Parameter estimate | Stratified Hazard Ratio |
| Point estimate | 0.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.54 |
| upper limit | 0.91 |

Secondary: Percentage of Participants With Objective Response Rate (ORR) as Assessed by the Investigator Using RECIST v1.1 in the Global Population

| | |
|-----------------|---|
| End point title | Percentage of Participants With Objective Response Rate (ORR) as Assessed by the Investigator Using RECIST v1.1 in the Global Population ^[3] |
|-----------------|---|

End point description:

Objective response (OR) is defined as complete response (CR) or partial response (PR) as determined by the investigator according to RECIST v1.1.

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

End point timeframe:

Baseline until partial response (PR) or complete response (CR), whichever occurs first (up to approximately 23 months)

Notes:

[3] - 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 the endpoint.

| | | | | |
|-----------------------------------|--|---|--|--|
| End point values | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - Global | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 202 | 201 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 76.7 (70.29 to 82.38) | 74.1 (67.50 to 80.03) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | ORR Statistical Analysis |
| Comparison groups | Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global |
| Number of subjects included in analysis | 403 |
| 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 | 0.55 |
| upper limit | 1.37 |

Secondary: Duration of Response (DOR) as Assessed by the Investigator Using RECIST v1.1 in the Global Population

| | |
|-----------------|--|
| End point title | Duration of Response (DOR) as Assessed by the Investigator Using RECIST v1.1 in the Global Population ^[4] |
|-----------------|--|

End point description:

DOR is defined as the time interval from first occurrence of a documented objective response to the time of disease progression as determined by the investigator using RECIST v1.1 or death from any cause, whichever comes first.

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

End point timeframe:

First occurrence of PR or CR until PD or death, whichever occurs first (up to approximately 23 months)

Notes:

[4] - 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 the endpoint.

| | | | | |
|----------------------------------|--|---|--|--|
| End point values | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - Global | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 155 | 149 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 3.1 (2.9 to 3.9) | 4.1 (3.5 to 4.2) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | DOR Statistical Analysis |
| Comparison groups | Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global |
| Number of subjects included in analysis | 304 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0063 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.715 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.562 |
| upper limit | 0.911 |

Secondary: PFS Rate at 6 Months and at 1 year in Global Population

| | |
|------------------------|---|
| End point title | PFS Rate at 6 Months and at 1 year in Global Population ^[5] |
| End point description: | PFS rates at 6 months and at 1 year is defined as the proportion of participants who are alive without disease progression 6 months and 1 year after randomization, respectively. |
| End point type | Secondary |
| End point timeframe: | 6 months, 1 year |

Notes:

[5] - 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 the endpoint.

| End point values | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - Global | | |
|-----------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 202 | 201 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 6 Months | 22.39 (16.56 to 28.22) | 30.86 (24.26 to 37.45) | | |
| 1 Year | 5.35 (2.14 to 8.56) | 12.62 (7.85 to 17.40) | | |

Statistical analyses

| | |
|-----------------------------------|--|
| Statistical analysis title | PFS Rate 1 Year Statistical Analysis |
| Statistical analysis description: | PFS Rate at 1 year |
| Comparison groups | Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global |

| | |
|---|-------------------------------|
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0133 |
| Method | Z-test |
| Parameter estimate | Difference in Event Free Rate |
| Point estimate | 7.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.52 |
| upper limit | 13.02 |

| | |
|---|--|
| Statistical analysis title | PFS Rate 6 Months Statistical Analysis |
| Statistical analysis description: | |
| PFS Rate at 6 months | |
| Comparison groups | Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global |
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0593 |
| Method | Z-test |
| Parameter estimate | Difference in Event Free Rate |
| Point estimate | 8.47 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.33 |
| upper limit | 17.27 |

| | |
|--|---|
| Secondary: OS Rate at 1 Year and 2 Years in the Global Population | |
| End point title | OS Rate at 1 Year and 2 Years in the Global Population ^[6] |
| End point description: | |
| OS rates at 1 and 2 years is defined as the proportion of participants who are alive 1 year and 2 years after randomization, respectively. Note: 999999=not estimable. | |
| End point type | Secondary |
| End point timeframe: | |
| 1 year, 2 years | |
| Notes: | |
| [6] - 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 the endpoint. | |

| End point values | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - Global | | |
|-----------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 202 | 201 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| 1 Year | 38.23 | 51.69 | | |
| 2 Years | 999999 | 999999 | | |

Statistical analyses

| Statistical analysis title | OS Rate 1 Year Statistical Analysis |
|---|--|
| Statistical analysis description: | |
| OS Rate at 1 year | |
| Comparison groups | Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global |
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0095 |
| Method | Z-test |
| Parameter estimate | Difference in Event Free Rate |
| Point estimate | 13.46 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 3.29 |
| upper limit | 23.64 |

Secondary: Time to Deterioration (TTD) per European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ) Core 30 (C30) Score in the Global Population

| | |
|-----------------|--|
| End point title | Time to Deterioration (TTD) per European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ) Core 30 (C30) Score in the Global Population ^[7] |
|-----------------|--|

End point description:

TTD according to the EORTC QLQ-C30 and EORTC QLQ-LC13 measures were evaluated in each of the following linearly transformed symptom scores: cough, dyspnea (single item), dyspnea (multi-item subscale), chest pain, or arm/shoulder pain. The linear transformation gives each individual symptom subscale a possible score of 0 to 100. For the symptom to be considered "deteriorated," a score increase of ≥ 10 points above baseline must be held for at least two consecutive assessments or an initial score increase of ≥ 10 points is followed by death within 3 weeks from the last assessment. A ≥ 10 -point change in the symptoms subscale score is perceived by participants as clinically significant. Note: 999999=not estimable; 000000=not estimable.

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

End point timeframe:

Baseline until deterioration per symptom subscale (up to approximately 23 months)

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 the endpoint.

| End point values | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - Global | | |
|----------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 202 | 201 | | |
| Units: Month | | | | |
| median (confidence interval 95%) | | | | |
| Cough | 999999 (16.6 to 999999) | 20.3 (000000 to 999999) | | |
| Pain in Chest | 999999 (10.9 to 999999) | 999999 (999999 to 999999) | | |
| Pain in Arm or Shoulder | 999999 (8.8 to 999999) | 999999 (9.2 to 999999) | | |
| Dyspnea | 5.6 (3.6 to 8.8) | 999999 (5.5 to 999999) | | |

Statistical analyses

| Statistical analysis title | TTD Statistical Analysis Cough |
|--|--|
| Statistical analysis description: Cough | |
| Comparison groups | Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global |
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[8] |
| P-value | = 0.3604 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.221 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.795 |
| upper limit | 1.874 |

Notes:

[8] - Stratified analysis. Stratification factors: Sex (male vs female) and ECOG (0 vs 1).

| Statistical analysis title | TTD Statistical Analysis Pain in Arm or Shoulder |
|--|--|
| Statistical analysis description: Pain in Arm or Shoulder | |
| Comparison groups | Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global |

| | |
|---|-------------------|
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.6922 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.077 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.747 |
| upper limit | 1.552 |

| | |
|---|--|
| Statistical analysis title | TTD Statistical Analysis Dyspnea |
| Statistical analysis description: | |
| Dyspnea | |
| Comparison groups | Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global |
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.065 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.748 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.549 |
| upper limit | 1.019 |

| | |
|---|--|
| Statistical analysis title | TTD Statistical Analysis Pain in Chest |
| Statistical analysis description: | |
| Pain in Chest | |
| Comparison groups | Placebo + Carboplatin + Etoposide - Global v Atezolizumab + Carboplatin + Etoposide - Global |
| Number of subjects included in analysis | 403 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[9] |
| P-value | = 0.7712 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.058 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.722 |
| upper limit | 1.553 |

Notes:

[9] - Stratified analysis. Stratification factors: Sex (male vs female) and ECOG (0 vs 1).

Secondary: Percentage of Participants with at Least One Adverse Event in the Global Population

| | |
|-----------------|---|
| End point title | Percentage of Participants with at Least One Adverse Event in the Global Population ^[10] |
|-----------------|---|

End point description:

The percentage of participants with at least one adverse event in the global population.

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

End point timeframe:

Baseline until up to 90 days after end of treatment (up to approximately 49 months)

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 the endpoint.

| End point values | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - Global | | |
|-----------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 196 | 198 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 96.4 | 100.0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anti-Drug Antibodies (ADA) to Atezolizumab in the Global Population

| | |
|-----------------|---|
| End point title | Percentage of Participants With Anti-Drug Antibodies (ADA) to Atezolizumab in the Global Population ^[11] |
|-----------------|---|

End point description:

The baseline prevalence and post-baseline incidence of ADAs against atezolizumab.

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

End point timeframe:

Predose (0 hours [H]) on Day (D) 1 of Cycles (C) 1, 2, 3, 4, 8, 16, and every 8 cycles (Q8C) thereafter (cycle = 21 days) until treatment discontinuation (up to 23 months) and 120 days after last dose (up to approximately 23 months overall)

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: No statistical analysis for the endpoint.

| | | | | |
|--|---|--|--|--|
| End point values | Atezolizumab + Carboplatin + Etoposide - Global | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 198 | | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline evaluable participants (n=196) | 2.0 | | | |
| Post-baseline evaluable participants (n=188) | 18.6 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) of Atezolizumab in the Global Population

| | |
|-----------------|--|
| End point title | Maximum Observed Serum Concentration (Cmax) of Atezolizumab in the Global Population ^[12] |
|-----------------|--|

End point description:

Atezolizumab maximum observed plasma concentration (Cmax; 30 minutes following the end of the atezolizumab infusion) for each respective day.

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

End point timeframe:

Post-dose Day 1 of Cycle 1 (cycle length = 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: No statistical analysis for the endpoint.

| | | | | |
|--------------------------------------|---|--|--|--|
| End point values | Atezolizumab + Carboplatin + Etoposide - Global | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 185 | | | |
| Units: µg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 | 389 (± 135) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Serum Concentration (Cmin) of Atezolizumab in the Global Population

| | |
|-----------------|--|
| End point title | Minimum Observed Serum Concentration (Cmin) of Atezolizumab in the Global Population ^[13] |
|-----------------|--|

End point description:

Atezolizumab pre-dose plasma concentration (Cmin) for each respective day. Note: 999999=not estimable.

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

End point timeframe:

Predose on Day 1 of Cycles 1, 3, 4, 8, 16 and 24 (cycle length = 21 days)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for the endpoint.

| End point values | Atezolizumab + Carboplatin + Etoposide - Global | | | |
|--------------------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 194 | | | |
| Units: µg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 (n=194) | 999999 (± 999999) | | | |
| Cycle 3 Day 1 (n=174) | 80.6 (± 32.1) | | | |
| Cycle 4 Day 1 (n=156) | 138 (± 56.4) | | | |
| Cycle 8 Day 1 (n=88) | 186 (± 73.5) | | | |
| Cycle 16 Day 1 (n=22) | 196 (± 63.1) | | | |
| Cycle 24 Day 1 (n=4) | 221 (± 43.4) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Carboplatin in the Global Population

| | |
|-----------------|--|
| End point title | Plasma Concentration of Carboplatin in the Global Population ^[14] |
|-----------------|--|

End point description:

Plasma concentration of carboplatin in the Global population. Note: 999999=not estimable, D=Day, C=Cycle.

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

End point timeframe:

Predose, before end of infusion, and after end of carboplatin infusion on Day 1 of Cycle 1 and Cycle 3 (cycle = 21 days)

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: No statistical analysis for the endpoint.

| End point values | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - Global | | |
|---|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 13 | 13 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pre-Dose on D1 of C1 (n=12, 11) | 999999 (± 999999) | 999999 (± 999999) | | |
| Before End of Infusion on D1 of C1 (n=12, 11) | 13300 (± 4880) | 11200 (± 5060) | | |
| Post Infusion on D1 of C1 (n=11, 12) | 7200 (± 1880) | 6860 (± 1670) | | |
| Pre-Dose on D1 of C3 (n=12, 13) | 144 (± 58.3) | 126 (± 48.1) | | |
| Before End of Infusion on D1 of C3 (n=13, 13) | 13900 (± 3590) | 11300 (± 5090) | | |
| Post Infusion on D1 of C3 (n=13, 13) | 7180 (± 1630) | 6540 (± 2200) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Etoposide in the Global Population

| | |
|-----------------|--|
| End point title | Plasma Concentration of Etoposide in the Global Population ^[15] |
|-----------------|--|

End point description:

Plasma concentration of etoposide in the Global Population. Note: 999999=not estimable, C=Cycle, D=Day.

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

End point timeframe:

Predose, before end of infusion, 1 and 4 hours after end of carboplatin infusion on Day 1 of Cycle 1 and Cycle 3 (cycle = 21 days)

Notes:

[15] - 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 the endpoint.

| End point values | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - Global | | |
|---|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 13 | 13 | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pre-Dose on D1 of C1 (n=12, 13) | 999999 (± 999999) | 999999 (± 999999) | | |
| Before End of Infusion on D1 of C1 (n=10, 10) | 17000 (± 3640) | 19400 (± 2860) | | |
| 1 Hour Post Infusion on D1 of C1 (n=8, 12) | 11100 (± 2010) | 12600 (± 1960) | | |
| 4 Hours Post Infusion on D1 of C1 (n=9, 9) | 7640 (± 2360) | 7300 (± 1230) | | |
| Pre-Dose on D1 of C3 (n=13, 13) | 999999 (± 999999) | 999999 (± 999999) | | |

| | | | | |
|---|----------------|----------------|--|--|
| Before End of Infusion on D1 of C3 (n=11, 9) | 16600 (± 2180) | 17700 (± 3600) | | |
| 1 Hour Post Infusion on D1 of C3 (n=10, 13) | 12400 (± 3740) | 12200 (± 2810) | | |
| 4 Hours Post Infusion on D1 of C3 (n=10, 11) | 6740 (± 1230) | 7960 (± 2090) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first study drug administration to the data cutoff date: 7 July 2022 (up to 49 months).

Adverse event reporting additional description:

Adverse events reported based on safety population, which included participants who received any amount of any component of study treatment.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Placebo + Carboplatin + Etoposide - Global |
|-----------------------|--|

Reporting group description:

Participants in the Global population received intravenous infusions of placebo in combination with carboplatin to achieve an initial target AUC of 5 mg/mL/min followed by etoposide 100 mg/m² on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m² was administered alone. Thereafter, participants received maintenance (Cycle 5 onward) placebo on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

| | |
|-----------------------|--|
| Reporting group title | Atezolizumab + Carboplatin + Etoposide - China |
|-----------------------|--|

Reporting group description:

Participants in the China population received intravenous infusions of atezolizumab 1200 milligrams (mg) in combination with carboplatin to achieve an initial target area under the concentration-time curve (AUC) of 5 milligrams per milliliter per minute (mg/mL/min) followed by etoposide 100 milligrams per square meter (mg/m²) on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m² was administered alone. Thereafter, participants received maintenance (Cycle 5 onward) atezolizumab 1200 mg on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

| | |
|-----------------------|---|
| Reporting group title | Placebo + Carboplatin + Etoposide - China |
|-----------------------|---|

Reporting group description:

Participants in the China population received intravenous infusions of placebo in combination with carboplatin to achieve an initial target AUC of 5 mg/mL/min followed by etoposide 100 mg/m² on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m² was administered alone. Thereafter, participants received maintenance (Cycle 5 onward) placebo on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

| | |
|-----------------------|---|
| Reporting group title | Atezolizumab + Carboplatin + Etoposide - Global |
|-----------------------|---|

Reporting group description:

Participants in the Global population received intravenous infusions of atezolizumab 1200 milligrams (mg) in combination with carboplatin to achieve an initial target area under the concentration-time curve (AUC) of 5 milligrams per milliliter per minute (mg/mL/min) followed by etoposide 100 milligrams per square meter (mg/m²) on Day 1 of every 21-day cycle during the induction phase (Cycles 1-4). On Days 2 and 3 of every 21-day cycle during the induction phase (Cycles 1-4), etoposide 100 mg/m² was administered alone. Thereafter, participants received maintenance (Cycle 5 onward) atezolizumab 1200 mg on Day 1 of every 21-day cycle until persistent radiographic PD, symptomatic deterioration, intolerable toxicity, withdrawal of consent, death, or study termination by the Sponsor.

| Serious adverse events | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - China | Placebo + Carboplatin + Etoposide - China |
|---|--|--|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 69 / 196 (35.20%) | 22 / 57 (38.60%) | 14 / 52 (26.92%) |
| number of deaths (all causes) | 164 | 48 | 46 |
| number of deaths resulting from adverse events | 3 | 2 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Plasma cell myeloma | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paraneoplastic syndrome | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastatic neoplasm | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour pain | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral artery occlusion | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Superior vena cava syndrome | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Death | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 2 / 57 (3.51%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Systemic inflammatory response syndrome | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthenia | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchial obstruction | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute respiratory failure | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Hypercapnia | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 0 / 57 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 2 / 196 (1.02%) | 2 / 57 (3.51%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Alcohol abuse | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 4 / 57 (7.02%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 2 / 2 | 4 / 4 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 2 / 57 (3.51%) | 2 / 52 (3.85%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood alkaline phosphatase increased | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Head injury | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infusion related reaction | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 2 / 196 (1.02%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Radiation oesophagitis | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiopulmonary failure | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 3 / 196 (1.53%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac tamponade | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coronary artery disease | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Trigeminal neuralgia | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Guillain-Barre syndrome | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord oedema | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Pancytopenia | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 4 / 196 (2.04%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 4 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 0 / 57 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 4 / 196 (2.04%) | 0 / 57 (0.00%) | 2 / 52 (3.85%) |
| occurrences causally related to treatment / all | 4 / 4 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 8 / 196 (4.08%) | 1 / 57 (1.75%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 8 / 8 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Granulocytopenia | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 9 / 196 (4.59%) | 1 / 57 (1.75%) | 2 / 52 (3.85%) |
| occurrences causally related to treatment / all | 9 / 9 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelosuppression | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer perforation | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal adhesions | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lip oedema | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Faeces discoloured | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 3 / 196 (1.53%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Proctitis | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune colitis | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diverticular perforation | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaundice | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|-----------------|----------------|----------------|
| Rash | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin toxicity | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tubulointerstitial nephritis | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Autoimmune thyroiditis | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inappropriate antidiuretic hormone secretion | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myelitis | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 10 / 196 (5.10%) | 4 / 57 (7.02%) | 4 / 52 (7.69%) |
| occurrences causally related to treatment / all | 3 / 11 | 3 / 7 | 4 / 5 |
| deaths causally related to treatment / all | 1 / 3 | 0 / 0 | 0 / 0 |
| Pyopneumothorax | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Device related sepsis | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Lung abscess | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary sepsis | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 1 / 52 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 4 / 196 (2.04%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Electrolyte imbalance | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Atezolizumab + Carboplatin + Etoposide - Global | | |
|---|---|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 81 / 198 (40.91%) | | |
| number of deaths (all causes) | 155 | | |
| number of deaths resulting from adverse events | 3 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Plasma cell myeloma | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Paraneoplastic syndrome | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metastatic neoplasm | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tumour pain | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral artery occlusion | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Superior vena cava syndrome | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Death | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |

| | | | | |
|---|-----------------|--|--|--|
| Pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Systemic inflammatory response syndrome | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chest pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyrexia | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Asthenia | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fatigue | | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | | |
| occurrences causally related to treatment / all | 1 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Influenza like illness | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Non-cardiac chest pain | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory, thoracic and mediastinal disorders | | | | |

| | | | | |
|---|-----------------|--|--|--|
| Pneumothorax | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemoptysis | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary oedema | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pleural effusion | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchial obstruction | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Asthma | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary embolism | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chronic obstructive pulmonary disease | | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute respiratory failure | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypercapnia | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonitis | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 4 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Psychiatric disorders | | | |
| Alcohol abuse | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Depression | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transaminases increased | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neutrophil count decreased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| C-reactive protein increased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood alkaline phosphatase increased | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood bilirubin increased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aspartate aminotransferase increased | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood creatinine increased | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| White blood cell count decreased | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Liver function test increased | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Head injury | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Radiation oesophagitis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Limb injury | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |

| | | | | |
|---|-----------------|--|--|--|
| Supraventricular tachycardia | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiopulmonary failure | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrial fibrillation | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac tamponade | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atrioventricular block complete | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Coronary artery disease | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Palpitations | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pericardial effusion | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Trigeminal neuralgia | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Guillain-Barre syndrome | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neuropathy peripheral | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal cord oedema | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukopenia | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | |
| occurrences causally related to treatment / all | 4 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 5 / 198 (2.53%) | | |
| occurrences causally related to treatment / all | 5 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Disseminated intravascular coagulation | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 7 / 198 (3.54%) | | |
| occurrences causally related to treatment / all | 7 / 7 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Granulocytopenia | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 5 / 198 (2.53%) | | |
| occurrences causally related to treatment / all | 4 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myelosuppression | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastric ulcer perforation | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal adhesions | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatitis acute | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nausea | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lip oedema | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal obstruction | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatitis | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Faeces discoloured | | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal pain | | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ileus | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Proctitis | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Autoimmune colitis | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 198 (1.52%) | | |
| occurrences causally related to treatment / all | 3 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diverticular perforation | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Drug-induced liver injury | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholangitis | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Jaundice | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin toxicity | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tubulointerstitial nephritis | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| Autoimmune thyroiditis | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Inappropriate antidiuretic hormone secretion | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myelitis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 12 / 198 (6.06%) | | |
| occurrences causally related to treatment / all | 5 / 15 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Pyopneumothorax | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device related sepsis | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung abscess | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cytomegalovirus infection | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyponatraemia | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Electrolyte imbalance | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Placebo + Carboplatin + Etoposide - Global | Atezolizumab + Carboplatin + Etoposide - China | Placebo + Carboplatin + Etoposide - China |
|---|--|--|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 187 / 196 (95.41%) | 56 / 57 (98.25%) | 52 / 52 (100.00%) |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 6 / 196 (3.06%) | 0 / 57 (0.00%) | 2 / 52 (3.85%) |
| occurrences (all) | 8 | 0 | 2 |

| | | | |
|--|-------------------|------------------|------------------|
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 5 / 196 (2.55%) | 5 / 57 (8.77%) | 2 / 52 (3.85%) |
| occurrences (all) | 5 | 5 | 2 |
| Asthenia | | | |
| subjects affected / exposed | 20 / 196 (10.20%) | 4 / 57 (7.02%) | 4 / 52 (7.69%) |
| occurrences (all) | 26 | 4 | 5 |
| Chest pain | | | |
| subjects affected / exposed | 14 / 196 (7.14%) | 5 / 57 (8.77%) | 4 / 52 (7.69%) |
| occurrences (all) | 14 | 5 | 4 |
| Oedema peripheral | | | |
| subjects affected / exposed | 7 / 196 (3.57%) | 1 / 57 (1.75%) | 0 / 52 (0.00%) |
| occurrences (all) | 8 | 1 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 51 / 196 (26.02%) | 6 / 57 (10.53%) | 0 / 52 (0.00%) |
| occurrences (all) | 67 | 8 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 16 / 196 (8.16%) | 13 / 57 (22.81%) | 4 / 52 (7.69%) |
| occurrences (all) | 18 | 19 | 7 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 28 / 196 (14.29%) | 14 / 57 (24.56%) | 10 / 52 (19.23%) |
| occurrences (all) | 33 | 20 | 12 |
| Haemoptysis | | | |
| subjects affected / exposed | 12 / 196 (6.12%) | 4 / 57 (7.02%) | 5 / 52 (9.62%) |
| occurrences (all) | 12 | 4 | 6 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 5 / 196 (2.55%) | 2 / 57 (3.51%) | 0 / 52 (0.00%) |
| occurrences (all) | 6 | 2 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 9 / 196 (4.59%) | 7 / 57 (12.28%) | 5 / 52 (9.62%) |
| occurrences (all) | 14 | 7 | 5 |
| Dyspnoea | | | |
| subjects affected / exposed | 17 / 196 (8.67%) | 2 / 57 (3.51%) | 2 / 52 (3.85%) |
| occurrences (all) | 18 | 2 | 2 |
| Psychiatric disorders | | | |

| | | | |
|--------------------------------------|-------------------|------------------|------------------|
| Insomnia | | | |
| subjects affected / exposed | 14 / 196 (7.14%) | 4 / 57 (7.02%) | 3 / 52 (5.77%) |
| occurrences (all) | 14 | 8 | 9 |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 5 / 196 (2.55%) | 11 / 57 (19.30%) | 9 / 52 (17.31%) |
| occurrences (all) | 7 | 15 | 16 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 3 / 196 (1.53%) | 1 / 57 (1.75%) | 3 / 52 (5.77%) |
| occurrences (all) | 3 | 2 | 4 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 6 / 57 (10.53%) | 4 / 52 (7.69%) |
| occurrences (all) | 0 | 18 | 5 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 2 / 57 (3.51%) | 4 / 52 (7.69%) |
| occurrences (all) | 1 | 2 | 4 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 45 / 196 (22.96%) | 41 / 57 (71.93%) | 33 / 52 (63.46%) |
| occurrences (all) | 80 | 107 | 85 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 3 / 196 (1.53%) | 4 / 57 (7.02%) | 3 / 52 (5.77%) |
| occurrences (all) | 3 | 8 | 3 |
| Protein urine present | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 3 / 52 (5.77%) |
| occurrences (all) | 0 | 1 | 4 |
| Blood glucose increased | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 3 / 57 (5.26%) | 3 / 52 (5.77%) |
| occurrences (all) | 0 | 3 | 3 |
| Platelet count decreased | | | |
| subjects affected / exposed | 30 / 196 (15.31%) | 24 / 57 (42.11%) | 14 / 52 (26.92%) |
| occurrences (all) | 41 | 40 | 26 |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 8 / 57 (14.04%) | 4 / 52 (7.69%) |
| occurrences (all) | 0 | 23 | 4 |
| Weight increased | | | |

| | | | |
|--|-------------------|------------------|------------------|
| subjects affected / exposed | 6 / 196 (3.06%) | 1 / 57 (1.75%) | 4 / 52 (7.69%) |
| occurrences (all) | 7 | 1 | 4 |
| Weight decreased | | | |
| subjects affected / exposed | 10 / 196 (5.10%) | 10 / 57 (17.54%) | 6 / 52 (11.54%) |
| occurrences (all) | 11 | 10 | 6 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 2 / 57 (3.51%) | 5 / 52 (9.62%) |
| occurrences (all) | 0 | 2 | 6 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 1 / 57 (1.75%) | 3 / 52 (5.77%) |
| occurrences (all) | 0 | 1 | 4 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 24 / 196 (12.24%) | 34 / 57 (59.65%) | 29 / 52 (55.77%) |
| occurrences (all) | 43 | 101 | 73 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 3 / 196 (1.53%) | 4 / 57 (7.02%) | 0 / 52 (0.00%) |
| occurrences (all) | 3 | 6 | 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 6 / 196 (3.06%) | 13 / 57 (22.81%) | 10 / 52 (19.23%) |
| occurrences (all) | 6 | 21 | 15 |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 8 / 196 (4.08%) | 1 / 57 (1.75%) | 1 / 52 (1.92%) |
| occurrences (all) | 9 | 1 | 1 |
| Cardiac disorders | | | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 196 (0.51%) | 1 / 57 (1.75%) | 4 / 52 (7.69%) |
| occurrences (all) | 2 | 1 | 4 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 11 / 196 (5.61%) | 2 / 57 (3.51%) | 2 / 52 (3.85%) |
| occurrences (all) | 14 | 2 | 2 |
| Headache | | | |
| subjects affected / exposed | 23 / 196 (11.73%) | 3 / 57 (5.26%) | 3 / 52 (5.77%) |
| occurrences (all) | 26 | 3 | 3 |
| Blood and lymphatic system disorders | | | |

| | | | |
|-----------------------------|-------------------|------------------|------------------|
| Anaemia | | | |
| subjects affected / exposed | 69 / 196 (35.20%) | 46 / 57 (80.70%) | 40 / 52 (76.92%) |
| occurrences (all) | 84 | 76 | 50 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 29 / 196 (14.80%) | 17 / 57 (29.82%) | 16 / 52 (30.77%) |
| occurrences (all) | 44 | 27 | 31 |
| Leukopenia | | | |
| subjects affected / exposed | 19 / 196 (9.69%) | 9 / 57 (15.79%) | 14 / 52 (26.92%) |
| occurrences (all) | 32 | 24 | 22 |
| Neutropenia | | | |
| subjects affected / exposed | 66 / 196 (33.67%) | 11 / 57 (19.30%) | 17 / 52 (32.69%) |
| occurrences (all) | 105 | 32 | 41 |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 58 / 196 (29.59%) | 10 / 57 (17.54%) | 8 / 52 (15.38%) |
| occurrences (all) | 70 | 19 | 12 |
| Abdominal distension | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 3 / 57 (5.26%) | 1 / 52 (1.92%) |
| occurrences (all) | 2 | 3 | 1 |
| Stomatitis | | | |
| subjects affected / exposed | 9 / 196 (4.59%) | 1 / 57 (1.75%) | 1 / 52 (1.92%) |
| occurrences (all) | 9 | 1 | 1 |
| Vomiting | | | |
| subjects affected / exposed | 34 / 196 (17.35%) | 14 / 57 (24.56%) | 7 / 52 (13.46%) |
| occurrences (all) | 49 | 20 | 7 |
| Abdominal pain | | | |
| subjects affected / exposed | 11 / 196 (5.61%) | 0 / 57 (0.00%) | 0 / 52 (0.00%) |
| occurrences (all) | 11 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 30 / 196 (15.31%) | 4 / 57 (7.02%) | 2 / 52 (3.85%) |
| occurrences (all) | 46 | 5 | 2 |
| Nausea | | | |
| subjects affected / exposed | 65 / 196 (33.16%) | 21 / 57 (36.84%) | 10 / 52 (19.23%) |
| occurrences (all) | 95 | 47 | 15 |
| Hepatobiliary disorders | | | |

| | | | |
|---|-------------------------|------------------------|------------------------|
| Hepatic function abnormal subjects affected / exposed occurrences (all) | 0 / 196 (0.00%) 0 | 3 / 57 (5.26%) 3 | 3 / 52 (5.77%) 3 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 69 / 196 (35.20%) 72 | 25 / 57 (43.86%) 26 | 18 / 52 (34.62%) 18 |
| Rash subjects affected / exposed occurrences (all) | 13 / 196 (6.63%) 15 | 6 / 57 (10.53%) 9 | 1 / 52 (1.92%) 1 |
| Pruritus subjects affected / exposed occurrences (all) | 9 / 196 (4.59%) 10 | 2 / 57 (3.51%) 3 | 1 / 52 (1.92%) 1 |
| Rash maculo-papular subjects affected / exposed occurrences (all) | 2 / 196 (1.02%) 3 | 0 / 57 (0.00%) 0 | 0 / 52 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Proteinuria subjects affected / exposed occurrences (all) | 1 / 196 (0.51%) 1 | 2 / 57 (3.51%) 3 | 7 / 52 (13.46%) 10 |
| Endocrine disorders | | | |
| Hypothyroidism subjects affected / exposed occurrences (all) | 1 / 196 (0.51%) 1 | 8 / 57 (14.04%) 9 | 2 / 52 (3.85%) 2 |
| Hyperthyroidism subjects affected / exposed occurrences (all) | 5 / 196 (2.55%) 5 | 2 / 57 (3.51%) 2 | 0 / 52 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain subjects affected / exposed occurrences (all) | 18 / 196 (9.18%) 20 | 3 / 57 (5.26%) 3 | 0 / 52 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 8 / 196 (4.08%) 9 | 2 / 57 (3.51%) 2 | 2 / 52 (3.85%) 2 |
| Arthralgia | | | |

| | | | |
|--|-------------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 22 / 196 (11.22%) 29 | 1 / 57 (1.75%) 1 | 4 / 52 (7.69%) 4 |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 6 / 196 (3.06%) | 2 / 57 (3.51%) | 5 / 52 (9.62%) |
| occurrences (all) | 6 | 5 | 5 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 17 / 196 (8.67%) | 3 / 57 (5.26%) | 2 / 52 (3.85%) |
| occurrences (all) | 20 | 3 | 2 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 3 / 57 (5.26%) | 4 / 52 (7.69%) |
| occurrences (all) | 2 | 3 | 4 |
| Metabolism and nutrition disorders | | | |
| Hypoproteinaemia | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 4 / 57 (7.02%) | 3 / 52 (5.77%) |
| occurrences (all) | 0 | 4 | 4 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 9 / 57 (15.79%) | 5 / 52 (9.62%) |
| occurrences (all) | 2 | 14 | 5 |
| Hypochloraemia | | | |
| subjects affected / exposed | 2 / 196 (1.02%) | 5 / 57 (8.77%) | 4 / 52 (7.69%) |
| occurrences (all) | 3 | 6 | 7 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 10 / 196 (5.10%) | 1 / 57 (1.75%) | 2 / 52 (3.85%) |
| occurrences (all) | 10 | 1 | 3 |
| Hyponatraemia | | | |
| subjects affected / exposed | 12 / 196 (6.12%) | 10 / 57 (17.54%) | 11 / 52 (21.15%) |
| occurrences (all) | 14 | 12 | 17 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 5 / 196 (2.55%) | 4 / 57 (7.02%) | 2 / 52 (3.85%) |
| occurrences (all) | 7 | 4 | 3 |
| Hypokalaemia | | | |
| subjects affected / exposed | 17 / 196 (8.67%) | 5 / 57 (8.77%) | 5 / 52 (9.62%) |
| occurrences (all) | 18 | 8 | 10 |
| Hypertriglyceridaemia | | | |

| | | | |
|-----------------------------|-------------------|------------------|------------------|
| subjects affected / exposed | 1 / 196 (0.51%) | 3 / 57 (5.26%) | 0 / 52 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 196 (0.00%) | 0 / 57 (0.00%) | 3 / 52 (5.77%) |
| occurrences (all) | 0 | 0 | 3 |
| Decreased appetite | | | |
| subjects affected / exposed | 41 / 196 (20.92%) | 13 / 57 (22.81%) | 12 / 52 (23.08%) |
| occurrences (all) | 45 | 22 | 16 |

| | | | |
|---|---|--|--|
| Non-serious adverse events | Atezolizumab + Carboplatin + Etoposide - Global | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 191 / 198 (96.46%) | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 15 / 198 (7.58%) | | |
| occurrences (all) | 20 | | |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 2 / 198 (1.01%) | | |
| occurrences (all) | 2 | | |
| Asthenia | | | |
| subjects affected / exposed | 25 / 198 (12.63%) | | |
| occurrences (all) | 29 | | |
| Chest pain | | | |
| subjects affected / exposed | 18 / 198 (9.09%) | | |
| occurrences (all) | 22 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 13 / 198 (6.57%) | | |
| occurrences (all) | 14 | | |
| Fatigue | | | |
| subjects affected / exposed | 52 / 198 (26.26%) | | |
| occurrences (all) | 66 | | |
| Pyrexia | | | |
| subjects affected / exposed | 20 / 198 (10.10%) | | |
| occurrences (all) | 32 | | |
| Respiratory, thoracic and mediastinal | | | |

| | | | |
|--------------------------------------|-------------------|--|--|
| disorders | | | |
| Cough | | | |
| subjects affected / exposed | 22 / 198 (11.11%) | | |
| occurrences (all) | 28 | | |
| Haemoptysis | | | |
| subjects affected / exposed | 14 / 198 (7.07%) | | |
| occurrences (all) | 20 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 13 / 198 (6.57%) | | |
| occurrences (all) | 17 | | |
| Productive cough | | | |
| subjects affected / exposed | 10 / 198 (5.05%) | | |
| occurrences (all) | 10 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 21 / 198 (10.61%) | | |
| occurrences (all) | 24 | | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 16 / 198 (8.08%) | | |
| occurrences (all) | 19 | | |
| Investigations | | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 8 / 198 (4.04%) | | |
| occurrences (all) | 9 | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 8 / 198 (4.04%) | | |
| occurrences (all) | 8 | | |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences (all) | 4 | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 37 / 198 (18.69%) | | |
| occurrences (all) | 74 | | |

| | | | |
|--|-------------------------|--|--|
| Blood creatinine increased subjects affected / exposed occurrences (all) | 7 / 198 (3.54%) 13 | | |
| Protein urine present subjects affected / exposed occurrences (all) | 0 / 198 (0.00%) 0 | | |
| Blood glucose increased subjects affected / exposed occurrences (all) | 0 / 198 (0.00%) 0 | | |
| Platelet count decreased subjects affected / exposed occurrences (all) | 26 / 198 (13.13%) 38 | | |
| Blood cholesterol increased subjects affected / exposed occurrences (all) | 0 / 198 (0.00%) 0 | | |
| Weight increased subjects affected / exposed occurrences (all) | 3 / 198 (1.52%) 3 | | |
| Weight decreased subjects affected / exposed occurrences (all) | 21 / 198 (10.61%) 21 | | |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 0 / 198 (0.00%) 0 | | |
| Electrocardiogram QT prolonged subjects affected / exposed occurrences (all) | 0 / 198 (0.00%) 0 | | |
| White blood cell count decreased subjects affected / exposed occurrences (all) | 18 / 198 (9.09%) 35 | | |
| Haemoglobin decreased subjects affected / exposed occurrences (all) | 1 / 198 (0.51%) 1 | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 6 / 198 (3.03%) 13 | | |

| | | | |
|--|--|--|--|
| Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all) | 10 / 198 (5.05%) 13 | | |
| Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all) | 2 / 198 (1.01%) 2 | | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) | 20 / 198 (10.10%) 23 25 / 198 (12.63%) 30 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) | 86 / 198 (43.43%) 101 31 / 198 (15.66%) 46 24 / 198 (12.12%) 44 71 / 198 (35.86%) 122 | | |
| Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Abdominal distension subjects affected / exposed occurrences (all) Stomatitis | 52 / 198 (26.26%) 65 5 / 198 (2.53%) 5 | | |

| | | | |
|--|-------------------|--|--|
| subjects affected / exposed | 11 / 198 (5.56%) | | |
| occurrences (all) | 11 | | |
| Vomiting | | | |
| subjects affected / exposed | 40 / 198 (20.20%) | | |
| occurrences (all) | 52 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 10 / 198 (5.05%) | | |
| occurrences (all) | 10 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 34 / 198 (17.17%) | | |
| occurrences (all) | 46 | | |
| Nausea | | | |
| subjects affected / exposed | 77 / 198 (38.89%) | | |
| occurrences (all) | 112 | | |
| Hepatobiliary disorders | | | |
| Hepatic function abnormal | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 73 / 198 (36.87%) | | |
| occurrences (all) | 75 | | |
| Rash | | | |
| subjects affected / exposed | 15 / 198 (7.58%) | | |
| occurrences (all) | 25 | | |
| Pruritus | | | |
| subjects affected / exposed | 15 / 198 (7.58%) | | |
| occurrences (all) | 17 | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 11 / 198 (5.56%) | | |
| occurrences (all) | 11 | | |
| Renal and urinary disorders | | | |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences (all) | 0 | | |
| Endocrine disorders | | | |

| | | | |
|--|-------------------------|--|--|
| Hypothyroidism subjects affected / exposed occurrences (all) | 20 / 198 (10.10%) 20 | | |
| Hyperthyroidism subjects affected / exposed occurrences (all) | 11 / 198 (5.56%) 11 | | |
| Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) | 19 / 198 (9.60%) 19 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 13 / 198 (6.57%) 13 | | |
| Arthralgia subjects affected / exposed occurrences (all) | 25 / 198 (12.63%) 31 | | |
| Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all) | 13 / 198 (6.57%) 18 | | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 15 / 198 (7.58%) 19 | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 4 / 198 (2.02%) 5 | | |
| Metabolism and nutrition disorders Hypoproteinaemia subjects affected / exposed occurrences (all) | 0 / 198 (0.00%) 0 | | |
| Hypoalbuminaemia subjects affected / exposed occurrences (all) | 3 / 198 (1.52%) 5 | | |
| Hypochloraemia subjects affected / exposed occurrences (all) | 0 / 198 (0.00%) 0 | | |

| | | | |
|-----------------------------|-------------------|--|--|
| Hypomagnesaemia | | | |
| subjects affected / exposed | 13 / 198 (6.57%) | | |
| occurrences (all) | 19 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 10 / 198 (5.05%) | | |
| occurrences (all) | 10 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 9 / 198 (4.55%) | | |
| occurrences (all) | 13 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 9 / 198 (4.55%) | | |
| occurrences (all) | 9 | | |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 198 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 198 (0.51%) | | |
| occurrences (all) | 1 | | |
| Decreased appetite | | | |
| subjects affected / exposed | 55 / 198 (27.78%) | | |
| occurrences (all) | 64 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---|
| 25 August 2016 | Protocol was amended to include change of phase from Phase III to Phase I/III. A secondary objective and corresponding outcome measure has been added to evaluate the efficacy of atezolizumab + carboplatin + etoposide compared with placebo + carboplatin + etoposide as measured by investigator-assessed time to response (TTR). TTR will be assessed in the intent-to-treat (ITT) population for patients who had an objective response as determined by the investigator according to RECIST v1.1. Clarifications were made around eligibility criteria and study conduct. |
| 29 August 2017 | Protocol was amended to include modifications to the statistical analysis plan and the timing for the efficacy analyses for progression-free survival (PFS) and overall survival (OS). |
| 06 March 2019 | Protocol was amended to include additional language to the end of study definition to clarify that if the Sponsor decides to terminate the study, subjects who are still receiving study treatment or are in survival follow-up may be enrolled into an extension study or non-interventional study. The timing of the interim and final analysis were modified to be aligned with the statistical analysis plan. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported