# Clinical trial results:
# A Phase III, Open-Label, Randomized Study of Atezolizumab (MPDL3280A, Anti-PD-L1 Antibody) in Combination With Carboplatin+Paclitaxel With or Without Bevacizumab Compared With Carboplatin + Paclitaxel + Bevacizumab in Chemotherapy-Naïve Patients With Stage IV Non-Squamous Non-Small Cell Lung Cancer

## Summary

| | |
|---|---|
| EudraCT number | 2014-003207-30 |
| Trial protocol | LV AT DE BE ES BG NL LT PT FR SK IT |
| Global end of trial date | 07 December 2020 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 12 September 2021 |
| First version publication date | 20 September 2020 |
| Version creation reason | |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | GO29436 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02366143 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Hoffmann-La Roche |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, |
| Public contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com |
| Scientific contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 42 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 December 2020 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 07 December 2020 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the safety and efficacy of atezolizumab in combination with carboplatin+paclitaxel with or without bevacizumab compared with treatment with carboplatin+paclitaxel+bevacizumab in chemotherapy-naive patients with Stage IV non-squamous non-small cell lung cancer (NSCLC).

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 | 31 March 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Argentina: 10 |
| Country: Number of subjects enrolled | Australia: 88 |
| Country: Number of subjects enrolled | Austria: 12 |
| Country: Number of subjects enrolled | Belgium: 16 |
| Country: Number of subjects enrolled | Bulgaria: 10 |
| Country: Number of subjects enrolled | Brazil: 27 |
| Country: Number of subjects enrolled | Canada: 6 |
| Country: Number of subjects enrolled | Switzerland: 14 |
| Country: Number of subjects enrolled | Chile: 44 |
| Country: Number of subjects enrolled | Germany: 94 |
| Country: Number of subjects enrolled | Spain: 138 |
| Country: Number of subjects enrolled | France: 72 |
| Country: Number of subjects enrolled | Italy: 50 |
| Country: Number of subjects enrolled | Japan: 93 |
| Country: Number of subjects enrolled | Lithuania: 3 |
| Country: Number of subjects enrolled | Latvia: 17 |
| Country: Number of subjects enrolled | Mexico: 9 |
| Country: Number of subjects enrolled | Netherlands: 39 |
| Country: Number of subjects enrolled | Peru: 9 |
| Country: Number of subjects enrolled | Portugal: 23 |

| | |
|---|---|
| Country: Number of subjects enrolled | Russian Federation: 37 |
| Country: Number of subjects enrolled | Singapore: 9 |
| Country: Number of subjects enrolled | Slovakia: 8 |
| Country: Number of subjects enrolled | Taiwan: 34 |
| Country: Number of subjects enrolled | Ukraine: 74 |
| Country: Number of subjects enrolled | United States: 266 |
| Worldwide total number of subjects | 1202 |
| EEA total number of subjects | 482 |

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) | 664 |
| From 65 to 84 years | 531 |
| 85 years and over | 7 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

This study included chemotherapy-naive subjects with metastatic non-squamous non-small cell lung cancer (NSCLC).

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Arm C |

Arm description:

Bevacizumab+Paclitaxel+Carboplatin

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

Dosage and administration details:

Bevacizumab was administered as IV infusion at a dose of 15 milligrams per kilogram (mg/kg) on Day 1 of each 21-day cycle until progressive disease, unacceptable toxicity, or death.

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

Dosage and administration details:

Paclitaxel was administered as IV infusion at a dose of 200 milligrams per square meter (mg/m^2) on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first.

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

Dosage and administration details:

Carboplatin was administered at area under the concentration-time curve (AUC) 6 milligrams per milliliter per minute (mg/mL/min) on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first.

| | |
|---|---|
| **Arm title** | Arm B |

Arm description:

Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin

| | |
|---|---|
| Arm type | Experimental |

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

Dosage and administration details:

Atezolizumab was administered as IV infusion at a dose of 1200 milligrams (mg) on Day 1 of each 21-day cycle until loss of clinical benefit.

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

Dosage and administration details:

Bevacizumab was administered as IV infusion at a dose of 15 milligrams per kilogram (mg/kg) on Day 1 of each 21-day cycle until progressive disease, unacceptable toxicity, or death.

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

Dosage and administration details:

Paclitaxel was administered as IV infusion at a dose of 200 milligrams per square meter (mg/m^2) on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first.

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

Dosage and administration details:

Carboplatin was administered at area under the concentration-time curve (AUC) 6 milligrams per milliliter per minute (mg/mL/min) on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first.

| | |
|---|---|
| **Arm title** | Arm A |

Arm description:

Atezolizumab+Paclitaxel+Carboplatin

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

Dosage and administration details:

Atezolizumab was administered as IV infusion at a dose of 1200 milligrams (mg) on Day 1 of each 21-day cycle until loss of clinical benefit.

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

Dosage and administration details:

Paclitaxel was administered as IV infusion at a dose of 200 milligrams per square meter (mg/m^2) on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first.

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

Dosage and administration details:

Carboplatin was administered at area under the concentration-time curve (AUC) 6 milligrams per milliliter per minute (mg/mL/min) on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first.

| **Number of subjects in period 1** | Arm C | Arm B | Arm A |
|---|---|---|---|
| Started | 400 | 400 | 402 |
| Completed | 0 | 0 | 0 |
| Not completed | 400 | 400 | 402 |
| PI Move and Site Closure | 1 | - | 1 |
| Physician decision | 1 | 2 | 1 |
| Patient moved to roll-over study | 1 | 19 | 28 |
| Patient switched to PTAP | - | 1 | - |
| Patient rolling over to patient assistance program | - | - | 1 |
| Sponsor request to withdraw/discontinue | - | 6 | - |
| Patient moving onto PTAP commercial stock | - | 1 | - |
| Stopped treatment due to disease progression | - | - | 1 |
| Continue same Tx via Post Trial Access Prog(PTAP) | - | - | 1 |
| Consent withdrawn by subject | 16 | 17 | 22 |
| Post Trial Migration | - | 1 | - |
| Patient moved to commercial atezolizumab use | - | 11 | 7 |
| Uneligible | - | 1 | - |
| Study Terminated By Sponsor | - | - | 2 |
| Death | 307 | 278 | 280 |
| Requester's instructions | 1 | 1 | 1 |
| Sponsor request discontinue in survival followup | 70 | 57 | 52 |
| Patient moved to commercial stock | - | - | 1 |
| Lost to follow-up | 2 | 4 | 2 |
| Randomization Error | 1 | - | - |
| Increased Microscopic RBCS on Urinalysis | - | 1 | - |
| Protocol deviation | - | - | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Arm C |
| Reporting group description: Bevacizumab+Paclitaxel+Carboplatin | |
| Reporting group title | Arm B |
| Reporting group description: Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin | |
| Reporting group title | Arm A |
| Reporting group description: Atezolizumab+Paclitaxel+Carboplatin | |

| Reporting group values | Arm C | Arm B | Arm A |
|---|---|---|---|
| Number of subjects | 400 | 400 | 402 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 226 | 215 | 223 |
| From 65-84 years | 171 | 182 | 178 |
| 85 years and over | 3 | 3 | 1 |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 63.1 | 63.0 | 62.3 |
| standard deviation | ± 9.3 | ± 9.5 | ± 9.2 |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 161 | 160 | 161 |
| Male | 239 | 240 | 241 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 3 | 0 |
| Asian | 46 | 56 | 48 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 12 | 3 | 9 |
| White | 335 | 322 | 331 |
| More than one race | 0 | 3 | 4 |
| Unknown or Not Reported | 6 | 13 | 10 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 1202 | | |

| | | | |
|---|---|---|---|
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 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) | 664 | | |
| From 65-84 years | 531 | | |
| 85 years and over | 7 | | |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 482 | | |
| Male | 720 | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 4 | | |
| Asian | 150 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 24 | | |
| White | 988 | | |
| More than one race | 7 | | |
| Unknown or Not Reported | 29 | | |

**Subject analysis sets**

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit

whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

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| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
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| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

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|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

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| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

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|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

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|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

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| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

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|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |

| | |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or

death.

| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
|---|---|
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or

until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| **Reporting group values** | Arm C (Bevacizumab+Paclitaxel+Carboplatin) | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
|---|---|---|---|
| Number of subjects | 336 | 359 | 337 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | ± | ± | ± |

| | | | |
|---|---|---|---|
| Sex: Female, Male<br>Units: Participants | | | |
| Female | | | |
| Male | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | | | |
| Asian | | | |
| Native Hawaiian or Other Pacific Islander | | | |
| Black or African American | | | |
| White | | | |
| More than one race | | | |
| Unknown or Not Reported | | | |

| **Reporting group values** | Arm A (Atezolizumab+Paclitaxel+Carboplatin) | Arm C (Bevacizumab+Paclitaxel+Carboplatin) | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
|---|---|---|---|
| Number of subjects | 350 | 338 | 400 |
| Age categorical<br>Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | ± |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | | | |
| Male | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | | | |
| Asian | | | |
| Native Hawaiian or Other Pacific Islander | | | |
| Black or African American | | | |
| White | | | |
| More than one race | | | |
| Unknown or Not Reported | | | |

| **Reporting group values** | Arm C (Bevacizumab+Paclitaxel+Carboplatin) | Arm A (Atezolizumab+Paclitaxel+Carboplatin) | Arm B (Atezolizumab+Bevacizumab+Paclitaxel |
|---|---|---|---|

| | | | + Carboplatin) |
|---|---|---|---|
| Number of subjects | 400 | 348 | 190 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Sex: Female, Male<br>Units: Participants | | | |
| Female<br>Male | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported | | | |

| **Reporting group values** | Arm C (Bevacizumab+Paclitaxel+Carboplatin) | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
|---|---|---|---|
| Number of subjects | 164 | 192 | 165 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |

| | | | |
|---|---|---|---|
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Sex: Female, Male<br>Units: Participants | | | |
| Female<br>Male | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported | | | |

| **Reporting group values** | Arm A (Atezolizumab+Paclitaxel+Carboplatin) | Arm A (Atezolizumab+Paclitaxel+Carboplatin) | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
|---|---|---|---|
| Number of subjects | 185 | 402 | 224 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Sex: Female, Male<br>Units: Participants | | | |
| Female<br>Male | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race | | | |

| | | | |
|---|---|---|---|
| Unknown or Not Reported | | | |

| **Reporting group values** | Arm C (Bevacizumab+Paclitaxel+Carboplatin) | Arm A (Atezolizumab+Paclitaxel+Carboplatin) | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
|---|---|---|---|
| Number of subjects | 159 | 347 | 353 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Sex: Female, Male<br>Units: Participants | | | |
| Female<br>Male | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported | | | |

| **Reporting group values** | Arm C (Bevacizumab+Paclitaxel+Carboplatin) | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
|---|---|---|---|
| Number of subjects | 331 | 235 | 196 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years) | | | |

| | | | |
|---|---|---|---|
| Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Sex: Female, Male<br>Units: Participants | | | |
| Female<br>Male | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported | | | |

| **Reporting group values** | Arm A (Atezolizumab+Paclitaxel+Carboplatin) | Arm C (Bevacizumab+Paclitaxel+Carboplatin) | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
|---|---|---|---|
| Number of subjects | 222 | 197 | 348 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Sex: Female, Male<br>Units: Participants | | | |
| Female<br>Male | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian | | | |

| | | | |
|---|---|---|---|
| Native Hawaiian or Other Pacific Islander | | | |
| Black or African American | | | |
| White | | | |
| More than one race | | | |
| Unknown or Not Reported | | | |

| **Reporting group values** | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) | Arm C (Bevacizumab+Paclitaxel+Carboplatin) | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
|---|---|---|---|
| Number of subjects | 356 | 336 | 400 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | | | |
| standard deviation | ± | ± | ± |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | | | |
| Male | | | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | | | |
| Asian | | | |
| Native Hawaiian or Other Pacific Islander | | | |
| Black or African American | | | |
| White | | | |
| More than one race | | | |
| Unknown or Not Reported | | | |

| **Reporting group values** | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) | Arm C (Bevacizumab+Paclitaxel+Carboplatin) | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
|---|---|---|---|
| Number of subjects | 393 | 394 | 389 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |

| | | | |
|---|---|---|---|
| Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | <br><br><br>± | <br><br><br>± | <br><br>4.6<br>± |
| Sex: Female, Male<br>Units: Participants | | | |
| Female<br>Male | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported | | | |

| **Reporting group values** | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
|---|---|---|---|
| Number of subjects | 376 | 345 | 28 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | <br><br>2.9<br>± | <br><br><br>± | <br><br><br>± |
| Sex: Female, Male<br>Units: Participants | | | |
| Female<br>Male | | | |

| | | | |
|---|---|---|---|
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported | | | |

| **Reporting group values** | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) | Arm C (Bevacizumab+Paclitaxel+Carboplatin) | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
|---|---|---|---|
| Number of subjects | 35 | 24 | 325 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | ± | ± | ± |
| Sex: Female, Male<br>Units: Participants | | | |
| Female<br>Male | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported | | | |

| **Reporting group values** | Arm C (Bevacizumab+Paclitaxel+Carboplatin) | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) | |
|---|---|---|---|
| Number of subjects | 348 | 356 | |

| | | | |
|---|---|---|---|
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age Continuous<br>Units: Years<br>arithmetic mean<br>standard deviation | ± | ± | |
| Sex: Female, Male<br>Units: Participants | | | |
| Female<br>Male | | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported | | | |

### End points reporting groups

| | |
|---|---|
| Reporting group title | Arm C |
| Reporting group description: Bevacizumab+Paclitaxel+Carboplatin | |
| Reporting group title | Arm B |
| Reporting group description: Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin | |
| Reporting group title | Arm A |
| Reporting group description: Atezolizumab+Paclitaxel+Carboplatin | |
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death. | |
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase. | |
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death. | |
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit. | |
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death. | |
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or | |

until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or

death.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm A (Atezolizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received intravenous (IV) infusion of atezolizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab during maintenance treatment phase until loss of clinical benefit.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

| | |
|---|---|
| Subject analysis set title | Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of bevacizumab on Day 1 of each 21-day cycle followed by IV infusion

of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of bevacizumab during maintenance treatment phase until progressive disease, unacceptable toxicity, or death.

| | |
|---|---|
| Subject analysis set title | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Participants received IV infusion of atezolizumab and bevacizumab on Day 1 of each 21-day cycle followed by IV infusion of paclitaxel and carboplatin on Day 1 of each 21-day cycle for 4 or 6 cycles or until loss of clinical benefit whichever occurs first, during induction treatment phase. Participants received IV infusion of atezolizumab until loss of clinical benefit and bevacizumab until progressive disease, unacceptable toxicity, or death during maintenance treatment phase.

## Primary: Progression Free Survival (PFS), as Determined by the Investigator in Arm B Versus Arm C in the Teff-high WT Population and ITT-WT Population

| | |
|---|---|
| End point title | Progression Free Survival (PFS), as Determined by the Investigator in Arm B Versus Arm C in the Teff-high WT Population and ITT-WT Population |

End point description:

Progression Free Survival (PFS), as Determined by the Investigator using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) in Arm B versus Arm C in the T-effector (Teff)-high wild type (WT) population and the intent-to-treat (ITT)-WT population.

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

End point timeframe:

Baseline until disease progression or death, whichever occurs first until data cut-off on 15 September 2017 (up to approximately 29 months)

| **End point values** | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 336 | 356 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Teff-high WT (Arm B n=155; Arm C=129) | 6.8 (5.9 to 7.4) | 11.3 (9.1 to 13.0) | | |
| ITT-WT (Arm B n=356; Arm C=336) | 6.8 (6.0 to 7.1) | 8.3 (7.7 to 9.8) | | |

## Statistical analyses

| **Statistical analysis title** | PFS Statistical Analysis |
|---|---|

Statistical analysis description:

ITT-WT population

| | |
|---|---|
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |

| | |
|---|---|
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[1] |
| P-value | < 0.0001 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.52 |
| upper limit | 0.74 |

Notes:

[1] - Stratified Analysis

| **Statistical analysis title** | PFS Statistical Analysis |
|---|---|

Statistical analysis description:

Teff-high WT Population

| | |
|---|---|
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | < 0.0001 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.38 |
| upper limit | 0.68 |

## Primary: Overall Survival (OS) in Arm B Versus Arm C in ITT-WT Population

| | |
|---|---|
| End point title | Overall Survival (OS) in Arm B Versus Arm C in ITT-WT Population |

End point description:

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

End point timeframe:

Baseline until death until data cut-off on 22 January 2018 (up to approximately 34 months)

| End point values | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 359 | 337 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 19.2 (17.0 to 23.8) | 14.7 (13.3 to 16.9) | | |

**Statistical analyses**

| Statistical analysis title | OS Statistical Analysis |
|---|---|
| Statistical analysis description: ITT-WT Population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 696 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[2] |
| P-value | = 0.0164 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.78 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 0.96 |

Notes:
[2] - Stratified Analysis

**Primary: Overall Survival (OS) in Arm A Versus Arm C in ITT-WT Population**

| End point title | Overall Survival (OS) in Arm A Versus Arm C in ITT-WT Population |
|---|---|
| End point description: Overall Survival (OS) in Arm A Versus Arm C in ITT-WT Population | |
| End point type | Primary |
| End point timeframe: Baseline until death (up approximately 53 months) | |

| End point values | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 350 | 338 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 19.0 (15.7 to 21.5) | 14.7 (12.9 to 17.1) | | |

### Statistical analyses

| Statistical analysis title | OS Statistical Analysis |
|---|---|
| Statistical analysis description: ITT-WT Population | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 688 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[3] |
| P-value | = 0.0528 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.842 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.707 |
| upper limit | 1.002 |

Notes:

[3] - Stratified Analysis

### Secondary: PFS, as Determined by the Independent Review Facility (IRF) in Arm B Versus Arm C in Teff-High-WT Population and ITT-WT Population

| End point title | PFS, as Determined by the Independent Review Facility (IRF) in Arm B Versus Arm C in Teff-High-WT Population and ITT-WT Population |
|---|---|
| End point description: PFS, as determined by the independent review facility (IRF) Using RECIST v1.1 in Arm B versus Arm C in the T-effector (Teff)-high wild type (WT) population and the intent-to-treat (ITT)-WT population. | |
| End point type | Secondary |
| End point timeframe: Baseline until disease progression or death, whichever occurs first (up to approximately 29 months) | |

| End point values | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 336 | 356 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Teff-high WT Population (Arm B n=155; Arm C n=129) | 7.0 (6.1 to 8.1) | 10.7 (8.4 to 13.0) | | |
| ITT-WT Population (Arm B n=356; Arm C n=336) | 7.0 (6.3 to 8.0) | 8.5 (7.7 to 9.7) | | |

## Statistical analyses

| Statistical analysis title | PFS Statistical Analysis |
|---|---|
| Statistical analysis description: Teff-high WT Population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[4] |
| P-value | = 0.0001 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.564 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.418 |
| upper limit | 0.76 |

Notes:

[4] - Stratified Analysis

| Statistical analysis title | PFS Statistical Analysis |
|---|---|
| Statistical analysis description: ITT-WT population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[5] |
| P-value | = 0.0002 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.71 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.59 |
| upper limit | 0.85 |

Notes:

[5] - Stratified Analysis

## Secondary: PFS, as Determined by the Investigator in Arm B Versus Arm C in Teff High Population and ITT Population

| | |
|---|---|
| End point title | PFS, as Determined by the Investigator in Arm B Versus Arm C in Teff High Population and ITT Population |

End point description:

PFS, as determined by the investigator according to RECIST v1.1, in Arm B versus C in the Teff high population and ITT population.

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

End point timeframe:

Baseline until disease progression or death, whichever occurs first (up to approximately 29 months)

| **End point values** | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 400 | 400 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Teff-high (Arm B n=166; Arm C=148) | 11.3 (9.1 to 13.0) | 6.8 (5.8 to 7.3) | | |
| ITT Population (Arm B n=400; Arm C=4008) | 8.3 (7.9 to 9.8) | 6.8 (6.0 to 7.1) | | |

### Statistical analyses

| **Statistical analysis title** | PFS Statistical Analysis |
|---|---|

Statistical analysis description:

Teff-high Population

| | |
|---|---|
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 800 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[6] |
| P-value | < 0.0001 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.492 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.374 |
| upper limit | 0.649 |

Notes:

[6] - Stratified Analysis

| **Statistical analysis title** | PFS Statistical Analysis |
|---|---|

Statistical analysis description:

ITT Population

| | |
|---|---|
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 800 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[7] |
| P-value | < 0.0001 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.517 |
| upper limit | 0.72 |

Notes:

[7] - Stratified Analysis

## Secondary: PFS, as Determined by the Investigator in Arm A Versus Arm B in Teff High-WT Population and ITT-WT Population

| | |
|---|---|
| End point title | PFS, as Determined by the Investigator in Arm A Versus Arm B in Teff High-WT Population and ITT-WT Population |

End point description:

PFS, as determined by the investigator according to RECIST v1.1, in Arm A versus B in the Teff high-WT population and ITT-WT population.

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

End point timeframe:

Baseline until disease progression or death, whichever occurs first (up to approximately 29 months)

| **End point values** | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 348 | 356 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Teff-high WT (Arm A n=161; Arm B n=155) | 6.3 (5.6 to 7.8) | 11.3 (9.1 to 13.0) | | |

| | | | | |
|---|---|---|---|---|
| ITT-WT (Arm A n=348; Arm C n=356) | 6.3 (5.6 to 7.0) | 8.3 (7.7 to 9.8) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: PFS, as Determined by the Investigator in Arm B Versus Arm C by PD-L1 Subgroup

| | |
|---|---|
| End point title | PFS, as Determined by the Investigator in Arm B Versus Arm C by PD-L1 Subgroup |

End point description:

PFS as Determined by the Investigator according to RECIST v1.1, in Arm B Versus Arm C by PD-L1 Subgroup: TC2/3 or 1C2/3 and TC1/2/3 or IC1/2/3 (ITT-WT Population)

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

End point timeframe:

Baseline until disease progression or death, whichever occurs first (up to approximately 29 months)

| **End point values** | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 190 | 164 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| TC2/3 or IC2/3 (Arm B n=129; Arm C n=115) | 11.1 (8.3 to 13.0) | 6.8 (5.8 to 7.7) | | |
| TC1/2/3 or IC1/2/3 (Arm B n=190; Arm C n=164) | 11.0 (8.3 to 12.5) | 6.8 (5.8 to 7.3) | | |

### Statistical analyses

| **Statistical analysis title** | PFS Statistical Analysis |
|---|---|

Statistical analysis description:

TC1/2/3 or IC1/2/3 Subgroup

| | |
|---|---|
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 354 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[8] |
| P-value | < 0.0001 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.486 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.386 |
| upper limit | 0.639 |

Notes:

[8] - Stratified Analysis

| **Statistical analysis title** | PFS Statistical Analysis |
|---|---|

Statistical analysis description:

TC2/3 or IC2/3 Subgroup

| | |
|---|---|
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 354 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[9] |
| P-value | < 0.0001 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.471 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.352 |
| upper limit | 0.647 |

Notes:

[9] - Stratified Analysis

## Secondary: OS in Arm B Versus Arm C by PD-L1 Subgroup

| | |
|---|---|
| End point title | OS in Arm B Versus Arm C by PD-L1 Subgroup |

End point description:

OS in Arm B Versus Arm C by PD-L1 Subgroup: TC2/3 or 1C2/3 and TC1/2/3 or IC1/2/3 (ITT-WT Population)

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

End point timeframe:

Baseline until death (up to approximately 34 months)

| **End point values** | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 192 | 165 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| TC 2/3 or IC2/3 (Arm B n=129; Arm C n=116) | 22.2 (17.0 to 26.1) | 16.7 (10.5 to 24.2) | | |
| TC1/2/3 or IC1/2/3 (Arm B n=192; Arm C n=165) | 22.5 (18.2 to 26.1) | 16.4 (11.2 to 22.9) | | |

### Statistical analyses

| **Statistical analysis title** | OS Analysis by PD-L1 Subgroup |
|---|---|
| Statistical analysis description:<br>TC2/3 or IC2/3, WT ITT | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[10] |
| P-value | = 0.2765 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.824 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.58 |
| upper limit | 1.169 |

Notes:

[10] - Unstratified Analysis

| **Statistical analysis title** | OS Analysis by PD-L1 Subgroup |
|---|---|
| Statistical analysis description:<br>TC1/2/3 or IC1/2/3, WT ITT | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[11] |
| P-value | = 0.0829 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.771 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.575 |
| upper limit | 1.035 |

Notes:

[11] - Unstratified Analysis

## Secondary: OS in Arm A Versus Arm C by PD-L1 Subgroup

| End point title | OS in Arm A Versus Arm C by PD-L1 Subgroup |
|---|---|

| | |
|---|---|
| End point description: | |
| OS in Arm A Versus Arm C by PD-L1 Subgroup: TC2/3 or 1C2/3 and TC1/2/3 or IC1/2/3 (ITT-WT Population) | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline until death (up approximately 53 months) | |

| **End point values** | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 165 | 185 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| TC2/3 or IC2/3 (Arm A n=124; Arm C n=116) | 17.0 (10.3 to 22.9) | 26.1 (20.5 to 40.0) | | |
| TC1/2/3 or IC1/2/3 (Arm A n=185; Arm C n=165) | 16.0 (11.2 to 20.1) | 24.4 (20.2 to 28.1) | | |

**Statistical analyses**

| **Statistical analysis title** | OS by PD-L1 Subgroup |
|---|---|
| Statistical analysis description: | |
| TC2/3 or IC2/3 Population | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 350 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[12] |
| P-value | = 0.0097 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.662 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.484 |
| upper limit | 0.907 |

Notes:

[12] - Unstratified Analysis

| **Statistical analysis title** | OS by PD-L1 Subgroup |
|---|---|
| Statistical analysis description: | |
| TC1/2/3 or IC1/2/3 ITT-WT | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |

| | |
|---|---|
| Number of subjects included in analysis | 350 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[13] |
| P-value | = 0.0073 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.709 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.551 |
| upper limit | 0.913 |

Notes:

[13] - Unstratified Analysis

## Secondary: OS in Arm B Versus Arm C in Teff High-WT Population, Teff High Population, and ITT Population

| | |
|---|---|
| End point title | OS in Arm B Versus Arm C in Teff High-WT Population, Teff High Population, and ITT Population |

End point description:

Note: 999999=Not estimable

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

End point timeframe:

Baseline until death (up to approximately 34 months)

| End point values | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 400 | 400 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Teff High-WT (Arm B n=156; Arm C n=129) | 25.0 (17.8 to 999999) | 16.7 (12.4 to 999999) | | |
| Teff High Population (Arm B n=166; Arm C n=148) | 25.2 (19.1 to 999999) | 16.7 (12.4 to 999999) | | |
| ITT Population (Arm B n=400; Arm C n=400) | 19.8 (17.4 to 24.2) | 14.9 (13.4 to 17.1) | | |

### Statistical analyses

| Statistical analysis title | OS Statistical Analysis |
|---|---|

Statistical analysis description:

Teff high-WT

| | |
|---|---|
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |

| | |
|---|---|
| Number of subjects included in analysis | 800 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[14] |
| P-value | = 0.2843 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.831 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.592 |
| upper limit | 1.167 |

Notes:

[14] - Stratified Analysis

| **Statistical analysis title** | OS Statistical Analysis |
|---|---|
| Statistical analysis description: | |
| Teff high | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 800 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[15] |
| P-value | = 0.1861 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.802 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.579 |
| upper limit | 1.113 |

Notes:

[15] - Stratified Analysis

| **Statistical analysis title** | OS Statistical Analysis |
|---|---|
| Statistical analysis description: | |
| ITT | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 800 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.006 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.764 |

| Confidence interval | |
|---|---|
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.63 |
| upper limit | 0.926 |

## Secondary: OS in Arm A Versus Arm C in Teff High-WT Population, Teff High Population, and ITT Population

| End point title | OS in Arm A Versus Arm C in Teff High-WT Population, Teff High Population, and ITT Population |
|---|---|

End point description:

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

End point timeframe:

Baseline until death (up approximately 53 months)

| **End point values** | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 400 | 402 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Teff-high WT (Arm A n=163; Arm C n=130) | 16.3 (11.2 to 22.3) | 21.3 (17.6 to 26.3) | | |
| Teff-high Population (Arm A n=177; Arm C n=148) | 16.7 (11.4 to 21.6) | 21.0 (17.1 to 26.0) | | |
| ITT Population (Arm A n=402; Arm C n=400) | 15.0 (13.4 to 17.1) | 19.0 (16.3 to 21.5) | | |

### Statistical analyses

| **Statistical analysis title** | OS Statistical Analysis |
|---|---|

Statistical analysis description:

Teff high-WT

| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
|---|---|
| Number of subjects included in analysis | 802 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[16] |
| P-value | = 0.0894 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.786 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.595 |
| upper limit | 1.038 |

Notes:

[16] - Stratified Analysis

| **Statistical analysis title** | OS Statistical Analysis |
|---|---|

Statistical analysis description:

ITT

| | |
|---|---|
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 802 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[17] |
| P-value | = 0.0681 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.861 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.733 |
| upper limit | 1.011 |

Notes:

[17] - Stratified Analysis

| **Statistical analysis title** | OS Statistical Analysis |
|---|---|

Statistical analysis description:

Teff high

| | |
|---|---|
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 802 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[18] |
| P-value | = 0.1276 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.815 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.626 |
| upper limit | 1.061 |

Notes:

[18] - Stratified Analysis

## Secondary: OS in Arm A Versus Arm B in Teff High-WT Population and ITT-WT Population

| | |
|---|---|
| End point title | OS in Arm A Versus Arm B in Teff High-WT Population and ITT- |

| | |
|---|---|
| | WT Population |

End point description:

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

End point timeframe:

Baseline until death (up approximately 53 months)

| **End point values** | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 359 | 350 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Teff High-WT (Arm A n=163; Arm B n=156) | 25.8 (19.1 to 32.6) | 21.3 (17.6 to 26.3) | | |
| ITT-WT (Arm A n=350; Arm B n=359) | 19.5 (17.0 to 22.2) | 19.0 (15.7 to 21.5) | | |

## Statistical analyses

| **Statistical analysis title** | OS Statistical Analysis |
|---|---|

Statistical analysis description:

Teff high-WT ITT

| | |
|---|---|
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) |
| Number of subjects included in analysis | 709 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[19] |
| P-value | = 0.4599 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.901 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.683 |
| upper limit | 1.188 |

Notes:

[19] - Stratified Analysis

## Secondary: Duration of Response (DOR), as Determined By Investigator in Arm B Versus Arm C

| | |
|---|---|
| End point title | Duration of Response (DOR), as Determined By Investigator in Arm B Versus Arm C |

End point description:

DOR, as determined by investigator according to RECIST v1.1 in Arm B versus Arm C in the Teff high-WT population and the ITT-WT population.

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

End point timeframe:

Baseline until disease progression or death, whichever occurs first (up to approximately 29 months)

| **End point values** | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 224 | 159 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Teff high-WT (Arm B n=106; Arm C n=68) | 11.2 (9.7 to 15.7) | 5.7 (4.9 to 7.0) | | |
| ITT-WT (Arm B n=224; Arm C n=159) | 9.0 (6.9 to 11.4) | 5.7 (5.1 to 6.5) | | |

## Statistical analyses

| **Statistical analysis title** | DOR Statistical Analysis |
|---|---|

Statistical analysis description:

Teff-high WT

| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
|---|---|
| Number of subjects included in analysis | 383 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[20] |
| P-value | < 0.0001 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.283 |
| upper limit | 0.624 |

Notes:

[20] - Stratified Analysis

| **Statistical analysis title** | DOR Statistical Analysis |
|---|---|

Statistical analysis description:

ITT-WT

| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
|---|---|

| | |
|---|---|
| Number of subjects included in analysis | 383 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[21] |
| P-value | < 0.0001 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.523 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.406 |
| upper limit | 0.675 |

Notes:

[21] - Stratified Analysis

## Secondary: Percentage of Participants With an Objective Response (OR) (Complete Response [CR] or Partial Response [PR]) as Determined by the Investigator in the Teff-High-WT Population and ITT-WT Population

| | |
|---|---|
| End point title | Percentage of Participants With an Objective Response (OR) (Complete Response [CR] or Partial Response [PR]) as Determined by the Investigator in the Teff-High-WT Population and ITT-WT Population |

End point description:

Percentage of Participants With an Objective Response (OR) (Complete Response [CR] or Partial Response [PR]) as Determined by the Investigator using RECIST v1.1 in the Teff-High-WT population and ITT-WT population.

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

End point timeframe:

Baseline until disease progression or death, whichever occurs first (up to approximately 29 months)

| End point values | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 347 | 353 | 331 | |
| Units: Percentage | | | | |
| number (not applicable) | | | | |
| Teff-high WT (Arm A n=161; Arm B n=153) | 54.0 | 69.3 | 53.5 | |
| ITT-WT (Arm A n=347; Arm B n=353) | 49.3 | 63.5 | 48.0 | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: OS Rates at Years 1 and 2 in Arm B Versus Arm C

| | |
|---|---|
| End point title | OS Rates at Years 1 and 2 in Arm B Versus Arm C |

| | |
|---|---|
| End point description: | |
| OS at 1- and 2-year landmark timepoints in Teff-high WT population and ITT-WT population. | |
| End point type | Secondary |
| End point timeframe: | |
| Years 1 and 2 (up to approximately 34 months) | |

| **End point values** | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 235 | 196 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | | | | |
| 1-Year Teff-high WT (Arm B n=105; Arm C n=71) | 68.63 (61.28 to 75.98) | 58.74 (50.03 to 67.45) | | |
| 1-Year ITT-WT (Arm B n=235; Arm C n=196) | 67.32 (62.41 to 72.22) | 60.63 (55.34 to 65.93) | | |
| 2-Year Teff-high WT (Arm B n=21; Arm C n=15) | 52.03 (43.12 to 60.94) | 41.70 (31.55 to 51.85) | | |
| 2-Year ITT-WT (Arm B n=34; Arm C n=29) | 43.42 (36.94 to 49.90) | 33.71 (27.44 to 39.98) | | |

**Statistical analyses**

| **Statistical analysis title** | OS Rate at Year 1 Statistical Analysis |
|---|---|
| Statistical analysis description: | |
| 1-Year ITT-WT Population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 431 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[22] |
| P-value | = 0.0697 |
| Method | Z-test |
| Parameter estimate | Difference in Event Free Rate |
| Point estimate | 6.68 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.54 |
| upper limit | 13.9 |
| Notes: | |
| [22] - Stratified Analysis | |

| **Statistical analysis title** | OS Rate at Year 1 Statistical Analysis |
|---|---|
| Statistical analysis description: | |
| 1-Year Teff-high WT Population | |

| | |
|---|---|
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 431 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[23] |
| P-value | = 0.089 |
| Method | Z-test |
| Parameter estimate | Difference in Event Free Rate |
| Point estimate | 9.89 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.51 |
| upper limit | 21.29 |

Notes:

[23] - Stratified Analysis

| **Statistical analysis title** | OS Rate at Year 2 Statistical Analysis |
|---|---|
| Statistical analysis description: 2-Year Teff-high WT Population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 431 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[24] |
| P-value | = 0.1336 |
| Method | Z-test |
| Parameter estimate | Difference in Event Free Rate |
| Point estimate | 10.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.17 |
| upper limit | 23.84 |

Notes:

[24] - Stratified Analysis

| **Statistical analysis title** | OS Rate at Year 2 Statistical Analysis |
|---|---|
| Statistical analysis description: 2-Year ITT-WT Population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 431 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[25] |
| P-value | = 0.0347 |
| Method | Z-test |
| Parameter estimate | Difference in Event Free Rate |
| Point estimate | 9.71 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.7 |
| upper limit | 18.73 |

Notes:

[25] - Stratified Analysis

## Secondary: OS Rates at Years 1 and 2 in Arm A Versus Arm C

| | |
|---|---|
| End point title | OS Rates at Years 1 and 2 in Arm A Versus Arm C |

End point description:

OS at 1- and 2-year landmark timepoints in Teff-high WT population and ITT-WT population.

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

End point timeframe:

Years 1 and 2 (up to approximately 53 months)

| **End point values** | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 222 | 197 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | | | | |
| 1-Year Teff-high WT (Arm A n=110; Arm C n=72) | 67.48 (60.29 to 74.68) | 56.92 (48.32 to 65.53) | | |
| 2-Year Teff-high WT (Arm A n=75; Arm C n=49) | 46.01 (38.36 to 53.66) | 38.74 (30.26 to 47.22) | | |
| 1-Year ITT-WT (Arm A n=222; Arm C n=1972) | 64.06 (59.02 to 69.11) | 59.89 (54.61 to 65.17) | | |
| 2-Year ITT-WT (Arm A n=143; Arm C n=104) | 41.45 (36.26 to 46.64) | 31.79 (26.75 to 36.82) | | |

### Statistical analyses

| **Statistical analysis title** | OS Rate at Year 1 |
|---|---|

Statistical analysis description:

1-Year ITT-WT Population

| | |
|---|---|
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 419 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[26] |
| P-value | = 0.2624 |
| Method | Z-test |
| Parameter estimate | Difference in Event Free Rate |
| Point estimate | 4.18 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.13 |
| upper limit | 11.48 |

Notes:

[26] - Stratified Analysis

| **Statistical analysis title** | OS Rate at Year 2 |
|---|---|
| Statistical analysis description: | |
| 2-Year ITT-WT Population | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 419 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[27] |
| P-value | = 0.0088 |
| Method | Z-test |
| Parameter estimate | Difference in Event Free Rate |
| Point estimate | 9.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 2.43 |
| upper limit | 16.9 |

Notes:

[27] - Stratified Analysis

| **Statistical analysis title** | OS Rate at Year 1 |
|---|---|
| Statistical analysis description: | |
| 1-Year Teff-high WT Population | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 419 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[28] |
| P-value | = 0.0649 |
| Method | Z-test |
| Parameter estimate | Difference in Event Free Rate |
| Point estimate | 10.56 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.65 |
| upper limit | 21.77 |

Notes:

[28] - Stratified Analysis

| **Statistical analysis title** | OS Rate at Year 2 |
|---|---|

| Statistical analysis description: | |
|---|---|
| 2-Year Teff-high WT Population | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 419 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[29] |
| P-value | = 0.212 |
| Method | Z-test |
| Parameter estimate | Difference in Event Free Rate |
| Point estimate | 7.27 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.15 |
| upper limit | 18.69 |

Notes:

[29] - Stratified Analysis

## Secondary: Time to Deterioration (TTD) in Patient-Reported Lung Cancer Symptoms Determined by European Organization for Research and Treatment of Cancer (EORTC) Quality-of-Life Questionnaire-Core 30 (QLQ-C30) Score

| End point title | Time to Deterioration (TTD) in Patient-Reported Lung Cancer Symptoms Determined by European Organization for Research and Treatment of Cancer (EORTC) Quality-of-Life Questionnaire-Core 30 (QLQ-C30) Score |
|---|---|

End point description:

EORTC QLQ-C30 is a validated & reliable self-report measure that consists of 30 questions that assess 5 aspects of patient functioning, 3 symptom scales, health/quality of life,and 6 single items. EORTC QLQ-C30 is scored according to the EORTC scoring manual. All EORTC scales and single-item measures are linearly transformed so that each score has a range of 0-100. A high score for a functional/global health status scale represents a high or healthy level of functioning/HRQoL;however a high score for a symptom scale or item represents a high level of symptomatology or problems. A ≥10-point change in the symptoms subscale score is perceived by patients as clinically significant (Osoba et al.1998). Dyspnea in Teff-high WT (Arm A n=161; Arm B n=155; Arm C n= 129). Dyspnea ITT-WT (Arm A n=348; Arm B n=356; Arm C n= 336) Note: 999999=not estimable

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

End point timeframe:

Baseline up to approximately 29 months

| **End point values** | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 336 | 348 | 356 | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Dyspnea in Teff-high WT | 999999 (999999 to 999999) | 999999 (999999 to 999999) | 999999 (999999 to 999999) | |

| | | | | |
|---|---|---|---|---|
| Dyspnea ITT-WT | 999999 (999999 to 999999) | 999999 (999999 to 999999) | 999999 (999999 to 999999) | |

**Statistical analyses**

| **Statistical analysis title** | TTD EORTC QLQ-C30 Score |
|---|---|
| Statistical analysis description: | |
| Teff-high WT Population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[30] |
| P-value | = 0.6899 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.909 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.571 |
| upper limit | 1.45 |

Notes:

[30] - Stratified Analysis

| **Statistical analysis title** | TTD EORTC QLQ-C30 Score |
|---|---|
| Statistical analysis description: | |
| ITT WT | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[31] |
| P-value | = 0.173 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.232 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.912 |
| upper limit | 1.665 |

Notes:

[31] - Stratified Analysis

| **Statistical analysis title** | TTD EORTC QLQ-C30 Score |
|---|---|
| Statistical analysis description: | |
| ITT WT | |

| | |
|---|---|
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 684 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[32] |
| P-value | = 0.6145 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.084 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.792 |
| upper limit | 1.483 |

Notes:

[32] - Stratified Analysis

| **Statistical analysis title** | TTD EORTC QLQ-C30 Score |
|---|---|

Statistical analysis description:

Teff-high WT Population

| | |
|---|---|
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 684 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[33] |
| P-value | = 0.1043 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.671 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.413 |
| upper limit | 1.089 |

Notes:

[33] - Stratified Analysis

## Secondary: TTD in Patient-Reported Lung Cancer Symptoms as Determined by EORTC Quality-of-Life Questionnaire-Core Lung Cancer Module 13 (QLQ-LC13) Score

| | |
|---|---|
| End point title | TTD in Patient-Reported Lung Cancer Symptoms as Determined by EORTC Quality-of-Life Questionnaire-Core Lung Cancer Module 13 (QLQ-LC13) Score |

End point description:

QLQ-LC13 incorporates 1 multiple-item scale & a series of single items.EORTC scales & single-item measures are linearly transformed so that each score has a range of 0-100.A high score for a functional/global health status scale represents a high or healthy level of functioning/HRQoL;a high score for a symptom scale or item represents a high level of symptomatology or problems.Cough in Teff-high WT(Arm A n=161;Arm B n=155;Arm C n=129).Dyspnea in Teff-high WT(Arm A n=161;Arm B n=155;Arm C n=129).Chest Pain in Teff-high WT (Arm A n=161;Arm B n=155;Arm C n=129).Arm and/or Shoulder Pain in Teff-high WT (Arm A n=161;Arm B n=155; Arm C n=129).Cough in ITT-WT(Arm A n=348;Arm B n=356;Arm C n=336).Dyspnea in ITT-WT (Arm A n=348; Arm B n=356;Arm C n=336).Arm and/or Shoulder Pain in ITT-WT(Arm A n=348;Arm B n=356;Arm C n=336).Pain in Chest in ITT-WT(Arm A n=348;Arm B n=356;Arm C n=336).Note: 999999=not estimable

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

End point timeframe:

Baseline up to approximately 29 months

| End point values | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 336 | 348 | 356 | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Cough in Teff-high WT | 999999 (999999 to 999999) | 999999 (999999 to 999999) | 999999 (21.0 to 999999) | |
| Dyspnea in Teff-high WT | 999999 (6.3 to 999999) | 999999 (5.6 to 999999) | 999999 (999999 to 999999) | |
| Chest Pain in Teff-high WT | 18.4 (18.4 to 999999) | 999999 (999999 to 999999) | 22.2 (22.2 to 999999) | |
| Arm and/or Shoulder Pain in Teff-high WT | 999999 (12.7 to 999999) | 999999 (18.3 to 999999) | 19.5 (12.5 to 999999) | |
| Cough in ITT-WT | 999999 (999999 to 999999) | 999999 (999999 to 999999) | 999999 (21.0 to 999999) | |
| Dyspnea in ITT-WT | 999999 (10.0 to 999999) | 21.9 (9.7 to 999999) | 999999 (999999 to 999999) | |
| Arm and/or Shoulder Pain in ITT-WT | 999999 (999999 to 999999) | 999999 (18.3 to 999999) | 19.5 (15.2 to 999999) | |
| Pain in Chest in ITT-WT | 999999 (18.4 to 999999) | 999999 (999999 to 999999) | 999999 (22.2 to 999999) | |

## Statistical analyses

| Statistical analysis title | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: Cough for Teff-high WT ITT population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[34] |
| P-value | = 0.8816 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.041 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.614 |
| upper limit | 1.763 |

Notes:

[34] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: | |
| Dyspnea in Teff-high WT Population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[35] |
| P-value | = 0.7578 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.936 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.616 |
| upper limit | 1.422 |

Notes:

[35] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: | |
| Cough for Teff-high WT ITT Population | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 684 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[36] |
| P-value | = 0.2995 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.741 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.419 |
| upper limit | 1.309 |

Notes:

[36] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|

| | |
|---|---|
| Statistical analysis description: | |
| Pain in Chest in Teff-high WT Population | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 684 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[37] |
| P-value | = 0.2381 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.729 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.43 |
| upper limit | 1.235 |

Notes:

[37] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: | |
| Pain in Chest in Teff-high WT Population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[38] |
| P-value | = 0.1289 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.659 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.383 |
| upper limit | 1.133 |

Notes:

[38] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: | |
| Dyspnea in Teff-high WT Population | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 684 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[39] |
| P-value | = 0.847 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.041 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.694 |
| upper limit | 1.56 |

Notes:

[39] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: | |
| Cough in ITT-WT Population | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 684 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[40] |
| P-value | = 0.5377 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.891 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.619 |
| upper limit | 1.284 |

Notes:

[40] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: | |
| Arm and/or Shoulder Pain in Teff-high WT | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 684 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[41] |
| P-value | = 0.1502 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.693 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.42 |
| upper limit | 1.145 |

Notes:

[41] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|

| | |
|---|---|
| Statistical analysis description: | |
| Cough in ITT-WT Population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[42] |
| P-value | = 0.9568 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.01 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.713 |
| upper limit | 1.43 |

Notes:

[42] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: | |
| Arm and/or Shoulder Pain in Teff-high WT | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[43] |
| P-value | = 0.7163 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.09 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.685 |
| upper limit | 1.732 |

Notes:

[43] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: | |
| Dyspnea in ITT-WT Population | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 684 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[44] |
| P-value | = 0.7149 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.05 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.809 |
| upper limit | 1.363 |

Notes:

[44] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: | |
| Dyspnea in ITT-WT Population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[45] |
| P-value | = 0.4012 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.893 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.685 |
| upper limit | 1.163 |

Notes:

[45] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: | |
| Arm and/or Shoulder Pain in ITT-WT | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[46] |
| P-value | = 0.7126 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.057 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.786 |
| upper limit | 1.422 |

Notes:

[46] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|

| | |
|---|---|
| Statistical analysis description: | |
| Arm and/or Shoulder Pain in ITT-WT | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 684 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[47] |
| P-value | = 0.6053 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.921 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.675 |
| upper limit | 1.258 |

Notes:

[47] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: | |
| Pain in Chest in ITT-WT Population | |
| Comparison groups | Arm B (Atezolizumab+Bevacizumab+Paclitaxel + Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 692 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[48] |
| P-value | = 0.3134 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.829 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.576 |
| upper limit | 1.194 |

Notes:

[48] - Stratified Analysis

| **Statistical analysis title** | TTD by EORTC QLQ-LC13 Score |
|---|---|
| Statistical analysis description: | |
| Pain in Chest in ITT-WT Population | |
| Comparison groups | Arm A (Atezolizumab+Paclitaxel+Carboplatin) v Arm C (Bevacizumab+Paclitaxel+Carboplatin) |
| Number of subjects included in analysis | 684 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[49] |
| P-value | = 0.6115 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.91 |

| Confidence interval | |
|---|---|
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.633 |
| upper limit | 1.309 |

Notes:

[49] - Stratified Analysis

## Secondary: Change From Baseline in Patient-Reported Lung Cancer Symptoms Score Using the Symptoms in Lung Cancer (SILC) Scale

| End point title | Change From Baseline in Patient-Reported Lung Cancer Symptoms Score Using the Symptoms in Lung Cancer (SILC) Scale |
|---|---|

End point description:

The SILC scale was used to assess patient-reported severity of lung cancer symptoms (chest pain, dyspnea, and cough). The SILC scale is a 9-item content validated self-report measure of lung cancer symptoms. It measures severity of cough, dyspnea, and chest pain with a symptom severity score. The SILC questionnaire comprises three individual symptoms (dyspnea, cough, chest pain) and are scored at the individual symptom level, thus have a dyspnea score, chest pain score, and cough score. Each individual symptom score is calculated as the average of responses for the symptom items [e.g. Chest Pain Score=mean (item 1; item 2)]. An increase in score is suggestive of a worsening in symptomology (i.e. frequency or severity). A score change of ≥0.3 points for the dyspnea and cough symptom scores is considered to be clinically significant; whereas a score change of ≥0.5 points for the chest pain score is considered to be clinically significant. Note: 999999=not available.

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

End point timeframe:

Baseline up to approximately 29 months

| **End point values** | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 0[50] | 0[51] | 0[52] | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Teff-high WT | ( to ) | ( to ) | ( to ) | |
| ITT WT | ( to ) | ( to ) | ( to ) | |

Notes:

[50] - No analysis due to psychometric properties in NSCLC population are being determined & quality issue.

[51] - No analysis due to psychometric properties in NSCLC population are being determined & quality issue.

[52] - No analysis due to psychometric properties in NSCLC population are being determined & quality issue.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Adverse Events

| End point title | Percentage of Participants With Adverse Events |
|---|---|

End point description:

Percentage of participants with at least one adverse event.

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

End point timeframe:

Baseline up to data cutoff date 7 December 2020 (up to approximately 68 months)

| **End point values** | Arm C | Arm B | Arm A | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 394 | 393 | 400 | |
| Units: Percentage | | | | |
| number (not applicable) | 99.0 | 98.2 | 97.8 | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Percentage of Participants With Anti-Therapeutic Antibodies (ATAs) to Atezolizumab**

| End point title | Percentage of Participants With Anti-Therapeutic Antibodies (ATAs) to Atezolizumab |
|---|---|

End point description:

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

End point timeframe:

Baseline up to approximately 29 months

| **End point values** | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 389 | 376 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 4.6 | 2.9 | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Maximum Observed Serum Concentration (Cmax) of Atezolizumab in Arm A and Arm B**

| End point title | Maximum Observed Serum Concentration (Cmax) of Atezolizumab in Arm A and Arm B |
|---|---|

End point description:

The predose samples will be collected on the same day of treatment administration. The infusion duration of atezolizumab will be of 30-60 minutes.

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

End point timeframe:

Day 1 of Cycle 1 and 3 (Cycle length=21 days)

| **End point values** | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 378 | 364 | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 (Arm A n=378, Arm B n=364) | 410 (± 157) | 414 (± 127) | | |
| Cycle 3 Day 1 (Arm A n=310, Arm B n=302) | 498 (± 160) | 540 (± 198) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Minimum Observed Serum Concentration (Cmin) of Atezolizumab Prior to Infusion in Arm A and Arm B

| End point title | Minimum Observed Serum Concentration (Cmin) of Atezolizumab Prior to Infusion in Arm A and Arm B |
|---|---|

End point description:

Note: 999999=not available

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

End point timeframe:

Day 21 of Cycles 1, 2 3, and 7 (Cycle length=21 days)

| **End point values** | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 354 | 345 | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 21 (Arm A n=354; Arm B n=345) | 76.4 (± 37.7) | 80.8 (± 41.4) | | |

| | | | | |
|---|---|---|---|---|
| Cycle 2 Day 21 (Arm A n=322; Arm B n=319) | 119 (± 55.7) | 130 (± 57.1) | | |
| Cycle 3 Day 21 (Arm A n=312; Arm B n=307) | 146 (± 58.9) | 160 (± 102) | | |
| Cycle 7 Day 21 (Arm A n=230; Arm B n=249) | 219 (± 89.6) | 220 (± 99.0) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma Concentrations for Carboplatin in Arm A, Arm B, and Arm C

| End point title | Plasma Concentrations for Carboplatin in Arm A, Arm B, and Arm C |
|---|---|

End point description:

Note: 999999=not available. BEOI=Before end of infusion. AI=After infusion.

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

End point timeframe:

Predose (same day of treatment administration), 5-10 minutes before end of carboplatin infusion, 1 h after carboplatin infusion (infusion duration=15 to 30 minutes) on D1 of Cy1,3 (Cycle length=21 days)

| End point values | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 28 | 35 | 24 | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cy1D1 Pre-dose (Arm A n=28;Arm B n=35;Arm C n=24) | 999999 (± 999999) | 999999 (± 999999) | 999999 (± 999999) | |
| Cy1D1 BEOI (Arm A n=26;Arm B n=32;Arm C n=24) | 18300 (± 9610) | 18300 (± 11900) | 17200 (± 9860) | |
| Cy1D1 AI (Arm A n=26;Arm B n=31;Arm C n=22) | 11700 (± 5570) | 13900 (± 14300) | 10100 (± 5320) | |
| Cy2D21 (Arm A n=19;Arm B n=27;Arm C n=17) | 176 (± 82.9) | 190 (± 113) | 143 (± 73.0) | |
| Cy3D1 BEOI (Arm A n=18;Arm B n=28;Arm C n=16) | 20900 (± 8330) | 18700 (± 9410) | 20600 (± 12900) | |
| Cy3D1 AI (Arm A n=20;Arm B n=27;Arm C n=17) | 11700 (± 6990) | 12200 (± 7480) | 10400 (± 4150) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Plasma Concentrations for Paclitaxel in Arm A, Arm B, and Arm C

| End point title | Plasma Concentrations for Paclitaxel in Arm A, Arm B, and Arm |
|---|---|

| | |
|---|---|
| | C |

End point description:

Note: 999999=not available. BEOI=Before end of infusion. AI=After infusion

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

End point timeframe:

Predose (same day of treatment administration), 5-10 minutes before end of paclitaxel infusion, 1 h after paclitaxel infusion (infusion duration=3 h) on D1 of Cy1,3 (Cycle length=21 days)

| **End point values** | Arm A (Atezolizumab +Paclitaxel+Carboplatin) | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 28 | 35 | 24 | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cy1D1 Pre-dose (Arm A n=28; Arm B n=35;Arm C n=24) | 999999 (± 999999) | 999999 (± 999999) | 999999 (± 999999) | |
| Cy1D1 BEOI (Arm A n=26;Arm B n=34;Arm C n=24) | 4850 (± 2800) | 6440 (± 3640) | 5560 (± 2590) | |
| Cy1D1 AI (Arm A n=27;Arm B n=32;Arm C n=23) | 2300 (± 2790) | 2490 (± 3020) | 1980 (± 1780) | |
| Cy2D21 (Arm A n=2;Arm B n=3; Arm C n=0) | 999999 (± 999999) | 999999 (± 999999) | 999999 (± 999999) | |
| Cy3D1 BEOI (Arm A n=19; Arm B n=25; Arm C n=16) | 5810 (± 3610) | 7810 (± 4510) | 7810 (± 5160) | |
| Cy3D1 AI (Arm A n=19;Arm B n=27;Arm C n=17) | 1800 (± 1660) | 2990 (± 5830) | 1930 (± 1380) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cmax of Bevacizumab in Arm B and Arm C

| End point title | Cmax of Bevacizumab in Arm B and Arm C |
|---|---|

End point description:

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

End point timeframe:

Cycle 1 Day 1 and Cycle 3 Day 1 (Cycle length=21 days)

| End point values | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 205 | 215 | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 (Arm A n=205; Arm C n=215) | 329 (± 129) | 323 (± 95.0) | | |
| Cycle 3 Day 1 (Arm A n=154; Arm C n=168) | 413 (± 126) | 430 (± 123) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cmin of Bevacizumab in Arm B and Arm C

| End point title | Cmin of Bevacizumab in Arm B and Arm C |
|---|---|
| End point description:<br>Note: 999999=not available | |
| End point type | Secondary |
| End point timeframe:<br>Cycle 1 Day 1 and Cycle 2 Day 21 (Cycle length=21 days) | |

| End point values | Arm B (Atezolizumab +Bevacizumab +Paclitaxel + Carboplatin) | Arm C (Bevacizumab +Paclitaxel+Carboplatin) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 325 | 348 | | |
| Units: mcg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 1 Day 1 (Arm A n=325; Arm B n=348) | 999999 (± 999999) | 999999 (± 999999) | | |
| Cycle 2 Day 21 (Arm A n=280; Arm B n=316) | 98.0 (± 50.9) | 90.4 (± 36.8) | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the first study drug to the data cutoff date 7 December 2020 (up to approximately 68 months)

Adverse event reporting additional description:

The safety population included all treated participants, defined as randomized participants who received any amount of any component of study treatment.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 23.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Arm C (Bev+CP) |

Reporting group description:

Bevacizumab+Paclitaxel+Carboplatin

| | |
|---|---|
| Reporting group title | Arm A (Atezo+CP) |

Reporting group description:

Atezolizumab+Paclitaxel+Carboplatin

| | |
|---|---|
| Reporting group title | Arm B (Atezo+Bev+CP) |

Reporting group description:

Atezolizumab+Bevacizumab+Paclitaxel+Carboplatin

| Serious adverse events | Arm C (Bev+CP) | Arm A (Atezo+CP) | Arm B (Atezo+Bev+CP) |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 142 / 394 (36.04%) | 170 / 400 (42.50%) | 190 / 393 (48.35%) |
| number of deaths (all causes) | 311 | 293 | 285 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| ADENOCARCINOMA GASTRIC | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| B-CELL LYMPHOMA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| BLADDER TRANSITIONAL CELL CARCINOMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MARROW HYPERPLASIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| METASTASES TO MENINGES | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| MENINGIOMA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| TUMOUR PAIN | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TUMOUR PSEUDOPROGRESSION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| BLADDER NEOPLASM | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| ANEURYSM | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| AORTIC DISSECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| ARTERIAL OCCLUSIVE DISEASE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 1 / 400 (0.25%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETIC VASCULAR DISORDER | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| EMBOLISM | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EMBOLISM VENOUS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| HAEMATOMA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERTENSION | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOTENSION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LYMPHOEDEMA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ORTHOSTATIC HYPOTENSION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL ARTERIAL OCCLUSIVE DISEASE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| PERIPHERAL ARTERY THROMBOSIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL VASCULAR DISORDER | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| THROMBOSIS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 1 / 400 (0.25%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| VENOUS THROMBOSIS LIMB | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| Surgical and medical procedures | | | |
| VERTEBROPLASTY | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 1 / 400 (0.25%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHEST PAIN | | | |
| subjects affected / exposed | 6 / 394 (1.52%) | 1 / 400 (0.25%) | 4 / 393 (1.02%) |
| occurrences causally related to treatment / all | 1 / 7 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CATHETER SITE ERYTHEMA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| COMPLICATION ASSOCIATED WITH DEVICE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEATH | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 1 / 400 (0.25%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 2 |
| GENERAL PHYSICAL HEALTH DETERIORATION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 394 (0.51%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| INFUSION SITE EXTRAVASATION | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PYREXIA | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 6 / 400 (1.50%) | 8 / 393 (2.04%) |
| occurrences causally related to treatment / all | 0 / 1 | 3 / 6 | 2 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PAIN | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| ANAPHYLACTIC REACTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DRUG HYPERSENSITIVITY | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERSENSITIVITY | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| ACUTE RESPIRATORY DISTRESS SYNDROME | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| ACUTE RESPIRATORY FAILURE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 3 / 400 (0.75%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| BRONCHOSTENOSIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHRONIC OBSTRUCTIVE PULMONARY DISEASE | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 3 / 400 (0.75%) | 3 / 393 (0.76%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| COUGH | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 3 / 393 (0.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| DYSPNOEA | | | |
| subjects affected / exposed | 6 / 394 (1.52%) | 4 / 400 (1.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 1 / 6 | 0 / 4 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EPISTAXIS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMOPTYSIS | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 3 / 400 (0.75%) | 8 / 393 (2.04%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 4 | 3 / 8 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 3 / 3 |
| HICCUPS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| HYPOXIA | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 2 / 400 (0.50%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| IMMUNE-MEDIATED PNEUMONITIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| INTERSTITIAL LUNG DISEASE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 3 / 400 (0.75%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PLEURISY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PLEURITIC PAIN | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| PNEUMONIA ASPIRATION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| PNEUMONITIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 8 / 400 (2.00%) | 7 / 393 (1.78%) |
| occurrences causally related to treatment / all | 0 / 0 | 8 / 8 | 7 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMOTHORAX | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 4 / 400 (1.00%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PULMONARY HAEMORRHAGE | | | |
| subjects affected / exposed | 4 / 394 (1.02%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 3 / 4 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 2 / 2 | 0 / 0 | 2 / 2 |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 8 / 394 (2.03%) | 8 / 400 (2.00%) | 5 / 393 (1.27%) |
| occurrences causally related to treatment / all | 5 / 8 | 0 / 8 | 2 / 5 |
| deaths causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 2 |
| PULMONARY NECROSIS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| PULMONARY OEDEMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| RESPIRATORY FAILURE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| ALCOHOL WITHDRAWAL SYNDROME | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| ANXIETY | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CONFUSIONAL STATE | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BIPOLAR DISORDER | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DELIRIUM | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| MENTAL STATUS CHANGES | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DELUSION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PSYCHOTIC DISORDER | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| SUICIDAL IDEATION | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLOOD LACTATE DEHYDROGENASE INCREASED | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BLOOD PRESSURE INCREASED | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| C-REACTIVE PROTEIN INCREASED | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 CONDITION ABNORMAL | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATIC ENZYME INCREASED | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LIPASE INCREASED | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUTROPHIL COUNT DECREASED | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRANSAMINASES INCREASED | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| TROPONIN INCREASED | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| WHITE BLOOD CELL COUNT DECREASED | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| ACCIDENTAL OVERDOSE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| FALL | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FEMUR FRACTURE | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 2 / 400 (0.50%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FRACTURE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HIP FRACTURE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HUMERUS FRACTURE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFUSION RELATED REACTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 3 / 400 (0.75%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROCEDURAL COMPLICATION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| RIB FRACTURE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPINAL COMPRESSION FRACTURE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| STERNAL FRACTURE | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| WOUND COMPLICATION | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| Cardiac disorders | | | |
| ACUTE MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 3 / 394 (0.76%) | 1 / 400 (0.25%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 2 / 400 (0.50%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ATRIAL FLUTTER | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 SECOND DEGREE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CARDIAC ARREST | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| CARDIAC FAILURE | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| CORONARY ARTERY DISEASE | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| CARDIAC FAILURE CONGESTIVE | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| LEFT VENTRICULAR DYSFUNCTION | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 2 / 400 (0.50%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| MYOCARDIAL ISCHAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| PERICARDIAL EFFUSION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERICARDITIS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| TACHYARRHYTHMIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| VENTRICULAR TACHYCARDIA | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| AUTOIMMUNE MYOCARDITIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| ATAXIA | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 1 / 400 (0.25%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CEREBRAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| CEREBRAL INFARCTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 394 (0.25%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| CEREBRAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 2 / 400 (0.50%) | 5 / 393 (1.27%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | 3 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| DEPRESSED LEVEL OF CONSCIOUSNESS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COGNITIVE DISORDER | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| DIZZINESS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DYSAESTHESIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIZZINESS POSTURAL | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| ENCEPHALOPATHY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 394 (0.25%) | 1 / 400 (0.25%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMORRHAGE INTRACRANIAL | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| FOCAL DYSCOGNITIVE SEIZURES | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEADACHE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ISCHAEMIC STROKE | | | |
| subjects affected / exposed | 4 / 394 (1.02%) | 2 / 400 (0.50%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 3 / 4 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| LOSS OF CONSCIOUSNESS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| METABOLIC ENCEPHALOPATHY | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUROPATHY PERIPHERAL | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PARTIAL SEIZURES | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 1 / 400 (0.25%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PRESYNCOPE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 0 / 400 (0.00%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| SEIZURE | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 2 / 400 (0.50%) | 5 / 393 (1.27%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | 1 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SOMNOLENCE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| SPINAL CORD COMPRESSION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| SYNCOPE | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| TRANSIENT ISCHAEMIC ATTACK | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEMIPARESIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 4 / 394 (1.02%) | 5 / 400 (1.25%) | 5 / 393 (1.27%) |
| occurrences causally related to treatment / all | 4 / 4 | 5 / 6 | 5 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BONE MARROW FAILURE | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| FEBRILE NEUTROPENIA | | | |
| subjects affected / exposed | 17 / 394 (4.31%) | 13 / 400 (3.25%) | 27 / 393 (6.87%) |
| occurrences causally related to treatment / all | 16 / 18 | 13 / 13 | 28 / 30 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 3 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| NEUTROPENIA | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 1 / 400 (0.25%) | 4 / 393 (1.02%) |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NORMOCHROMIC ANAEMIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PANCYTOPENIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 394 (0.51%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SPONTANEOUS HAEMATOMA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 1 / 400 (0.25%) | 6 / 393 (1.53%) |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | 6 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MYELOSUPPRESSION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| OPTIC NEUROPATHY | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 3 / 394 (0.76%) | 2 / 400 (0.50%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 1 / 3 | 2 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 LOWER | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COLITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 6 / 393 (1.53%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 5 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CONSTIPATION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COLITIS ISCHAEMIC | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIARRHOEA | | | |
| subjects affected / exposed | 3 / 394 (0.76%) | 8 / 400 (2.00%) | 10 / 393 (2.54%) |
| occurrences causally related to treatment / all | 3 / 3 | 7 / 8 | 6 / 11 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIVERTICULAR PERFORATION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DYSPHAGIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DUODENAL ULCER | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FAECALOMA | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| FOOD POISONING | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| GASTRIC HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTRITIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 4 / 393 (1.02%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GASTROINTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ILEUS PARALYTIC | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| GLOSSODYNIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTESTINAL ANGINA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| INGUINAL HERNIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTESTINAL HAEMORRHAGE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INTESTINAL INFARCTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| INTESTINAL OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| INTESTINAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| INTESTINAL PERFORATION | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 0 / 400 (0.00%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| IRRITABLE BOWEL SYNDROME | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LARGE INTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| LARGE INTESTINE PERFORATION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NAUSEA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 394 (0.76%) | 1 / 400 (0.25%) | 7 / 393 (1.78%) |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 1 | 6 / 7 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| OESOPHAGEAL FOOD IMPACTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| PANCREATITIS ACUTE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| VOMITING | | | |
| subjects affected / exposed | 3 / 394 (0.76%) | 4 / 400 (1.00%) | 5 / 393 (1.27%) |
| occurrences causally related to treatment / all | 3 / 3 | 3 / 5 | 4 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| CHOLANGITIS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 3 / 393 (0.76%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHOLELITHIASIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| CHOLANGITIS ACUTE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATITIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATOTOXICITY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATOMEGALY | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| Skin and subcutaneous tissue disorders | | | |
| DERMATITIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ERYTHEMA MULTIFORME | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 3 / 400 (0.75%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PEMPHIGOID | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| RASH | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 3 / 400 (0.75%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RASH MACULO-PAPULAR | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| Renal and urinary disorders | | | |
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 3 / 394 (0.76%) | 2 / 400 (0.50%) | 3 / 393 (0.76%) |
| occurrences causally related to treatment / all | 1 / 3 | 1 / 2 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GLOMERULONEPHROPATHY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HAEMATURIA | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| NEPHROLITHIASIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PRERENAL FAILURE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL FAILURE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 3 / 393 (0.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL IMPAIRMENT | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RENAL INJURY | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| URINARY TRACT OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| TUBULOINTERSTITIAL NEPHRITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| ADRENOCORTICAL INSUFFICIENCY ACUTE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| ADRENAL INSUFFICIENCY | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 1 / 400 (0.25%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIABETES INSIPIDUS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| HYPOPHYSITIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOTHYROIDISM | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SECONDARY ADRENOCORTICAL INSUFFICIENCY | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |

| | | | |
|---|---|---|---|
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 3 / 394 (0.76%) | 1 / 400 (0.25%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ARTHRALGIA | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 3 / 400 (0.75%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 1 / 2 | 2 / 3 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BONE PAIN | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| COMPARTMENT SYNDROME | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FLANK PAIN | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| MYALGIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| OSTEOLYSIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| SOFT TISSUE NECROSIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VERTEBRAL FORAMINAL STENOSIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| SPINAL PAIN | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| Infections and infestations | | | |
| ABDOMINAL SEPSIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| ANAL ABSCESS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BACTERAEMIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BACTERIAL INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BONE ABSCESS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| BURSITIS INFECTIVE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| BRONCHITIS | | | |
| subjects affected / exposed | 2 / 394 (0.51%) | 1 / 400 (0.25%) | 4 / 393 (1.02%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CHRONIC SINUSITIS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| CELLULITIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| CLOSTRIDIUM DIFFICILE INFECTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DIVERTICULITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 394 (0.25%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| EMPYEMA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENCEPHALITIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| ENDOCARDITIS BACTERIAL | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| ENTERITIS INFECTIOUS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| FEBRILE INFECTION | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| ENTEROCOLITIS BACTERIAL | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| GASTROENTERITIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| HAEMORRHAGIC PNEUMONIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| GASTROENTERITIS CLOSTRIDIAL | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| HEPATITIS A | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HERPES ZOSTER | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 0 / 393 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HEPATITIS C | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFECTED SKIN ULCER | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFECTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| INFECTIOUS PLEURAL EFFUSION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| KLEBSIELLA SEPSIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| INFLUENZA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| LARGE INTESTINE INFECTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| LOWER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 3 / 400 (0.75%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 4 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| NEUTROPENIC SEPSIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| OSTEOMYELITIS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| PAROTITIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PARAINFLUENZAE VIRUS INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PNEUMONIA | | | |
| subjects affected / exposed | 18 / 394 (4.57%) | 21 / 400 (5.25%) | 28 / 393 (7.12%) |
| occurrences causally related to treatment / all | 4 / 19 | 5 / 23 | 8 / 30 |
| deaths causally related to treatment / all | 1 / 3 | 0 / 2 | 0 / 1 |
| PNEUMONIA ADENOVIRAL | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| PNEUMONIA BACTERIAL | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 3 / 393 (0.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PROSTATIC ABSCESS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| PYOPNEUMOTHORAX | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RESPIRATORY SYNCYTIAL VIRUS BRONCHITIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| RESPIRATORY SYNCYTIAL VIRUS INFECTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| RESPIRATORY TRACT INFECTION FUNGAL | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 TRACT INFECTION | | | |
| subjects affected / exposed | 3 / 394 (0.76%) | 2 / 400 (0.50%) | 4 / 393 (1.02%) |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 2 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| SALMONELLOSIS | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| SCROTAL ABSCESS | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| SEPSIS | | | |
| subjects affected / exposed | 5 / 394 (1.27%) | 3 / 400 (0.75%) | 3 / 393 (0.76%) |
| occurrences causally related to treatment / all | 1 / 5 | 1 / 3 | 1 / 4 |
| deaths causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 0 |
| SEPTIC SHOCK | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 2 / 400 (0.50%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| STAPHYLOCOCCAL BACTERAEMIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| STAPHYLOCOCCAL INFECTION | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| TOOTH ABSCESS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 3 / 394 (0.76%) | 4 / 400 (1.00%) | 3 / 393 (0.76%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 4 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VASCULAR DEVICE INFECTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VIRAL INFECTION | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 3 / 393 (0.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| DEHYDRATION | | | |
| subjects affected / exposed | 6 / 394 (1.52%) | 3 / 400 (0.75%) | 7 / 393 (1.78%) |
| occurrences causally related to treatment / all | 3 / 6 | 2 / 3 | 7 / 9 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| FAILURE TO THRIVE | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPERCALCAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 0 / 393 (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 |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 0 / 400 (0.00%) | 0 / 393 (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 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 1 / 400 (0.25%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 1 / 394 (0.25%) | 1 / 400 (0.25%) | 2 / 393 (0.51%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| HYPOPHOSPHATAEMIA | | | |
| subjects affected / exposed | 0 / 394 (0.00%) | 0 / 400 (0.00%) | 1 / 393 (0.25%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| **Non-serious adverse events** | Arm C (Bev+CP) | Arm A (Atezo+CP) | Arm B (Atezo+Bev+CP) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 381 / 394 (96.70%) | 385 / 400 (96.25%) | 375 / 393 (95.42%) |
| Vascular disorders | | | |
| HYPERTENSION | | | |
| subjects affected / exposed | 87 / 394 (22.08%) | 16 / 400 (4.00%) | 104 / 393 (26.46%) |
| occurrences (all) | 102 | 16 | 149 |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 80 / 394 (20.30%) | 76 / 400 (19.00%) | 84 / 393 (21.37%) |
| occurrences (all) | 107 | 127 | 143 |
| CHEST PAIN | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 28 / 394 (7.11%) | 38 / 400 (9.50%) | 35 / 393 (8.91%) |
| occurrences (all) | 32 | 44 | 37 |
| FATIGUE | | | |
| subjects affected / exposed | 107 / 394 (27.16%) | 111 / 400 (27.75%) | 137 / 393 (34.86%) |
| occurrences (all) | 125 | 129 | 157 |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 24 / 394 (6.09%) | 10 / 400 (2.50%) | 38 / 393 (9.67%) |
| occurrences (all) | 27 | 10 | 42 |
| MALAISE | | | |
| subjects affected / exposed | 11 / 394 (2.79%) | 20 / 400 (5.00%) | 27 / 393 (6.87%) |
| occurrences (all) | 13 | 27 | 43 |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 19 / 394 (4.82%) | 29 / 400 (7.25%) | 35 / 393 (8.91%) |
| occurrences (all) | 20 | 33 | 42 |
| PAIN | | | |
| subjects affected / exposed | 17 / 394 (4.31%) | 22 / 400 (5.50%) | 26 / 393 (6.62%) |
| occurrences (all) | 17 | 23 | 31 |
| PYREXIA | | | |
| subjects affected / exposed | 34 / 394 (8.63%) | 53 / 400 (13.25%) | 67 / 393 (17.05%) |
| occurrences (all) | 44 | 66 | 88 |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 77 / 394 (19.54%) | 82 / 400 (20.50%) | 86 / 393 (21.88%) |
| occurrences (all) | 94 | 99 | 107 |
| DYSPHONIA | | | |
| subjects affected / exposed | 18 / 394 (4.57%) | 11 / 400 (2.75%) | 27 / 393 (6.87%) |
| occurrences (all) | 19 | 12 | 27 |
| DYSPNOEA | | | |
| subjects affected / exposed | 60 / 394 (15.23%) | 86 / 400 (21.50%) | 67 / 393 (17.05%) |
| occurrences (all) | 66 | 107 | 81 |
| EPISTAXIS | | | |
| subjects affected / exposed | 86 / 394 (21.83%) | 17 / 400 (4.25%) | 67 / 393 (17.05%) |
| occurrences (all) | 108 | 22 | 89 |
| HAEMOPTYSIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 18 / 394 (4.57%) | 16 / 400 (4.00%) | 21 / 393 (5.34%) |
| occurrences (all) | 21 | 27 | 24 |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 10 / 394 (2.54%) | 9 / 400 (2.25%) | 22 / 393 (5.60%) |
| occurrences (all) | 10 | 10 | 25 |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 22 / 394 (5.58%) | 23 / 400 (5.75%) | 31 / 393 (7.89%) |
| occurrences (all) | 23 | 23 | 31 |
| INSOMNIA | | | |
| subjects affected / exposed | 38 / 394 (9.64%) | 50 / 400 (12.50%) | 42 / 393 (10.69%) |
| occurrences (all) | 41 | 56 | 43 |
| DEPRESSION | | | |
| subjects affected / exposed | 13 / 394 (3.30%) | 15 / 400 (3.75%) | 25 / 393 (6.36%) |
| occurrences (all) | 13 | 16 | 26 |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 20 / 394 (5.08%) | 22 / 400 (5.50%) | 30 / 393 (7.63%) |
| occurrences (all) | 24 | 26 | 45 |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 18 / 394 (4.57%) | 22 / 400 (5.50%) | 30 / 393 (7.63%) |
| occurrences (all) | 19 | 29 | 48 |
| NEUTROPHIL COUNT DECREASED | | | |
| subjects affected / exposed | 34 / 394 (8.63%) | 33 / 400 (8.25%) | 49 / 393 (12.47%) |
| occurrences (all) | 72 | 64 | 87 |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 44 / 394 (11.17%) | 41 / 400 (10.25%) | 57 / 393 (14.50%) |
| occurrences (all) | 76 | 59 | 84 |
| WHITE BLOOD CELL COUNT DECREASED | | | |
| subjects affected / exposed | 20 / 394 (5.08%) | 17 / 400 (4.25%) | 26 / 393 (6.62%) |
| occurrences (all) | 39 | 27 | 42 |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 42 / 394 (10.66%) | 29 / 400 (7.25%) | 52 / 393 (13.23%) |
| occurrences (all) | 46 | 32 | 56 |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| DIZZINESS | | | |
| subjects affected / exposed | 26 / 394 (6.60%) | 28 / 400 (7.00%) | 27 / 393 (6.87%) |
| occurrences (all) | 31 | 39 | 34 |
| DYSGEUSIA | | | |
| subjects affected / exposed | 19 / 394 (4.82%) | 15 / 400 (3.75%) | 24 / 393 (6.11%) |
| occurrences (all) | 24 | 16 | 27 |
| NEUROPATHY PERIPHERAL | | | |
| subjects affected / exposed | 67 / 394 (17.01%) | 104 / 400 (26.00%) | 92 / 393 (23.41%) |
| occurrences (all) | 77 | 117 | 105 |
| HEADACHE | | | |
| subjects affected / exposed | 53 / 394 (13.45%) | 41 / 400 (10.25%) | 70 / 393 (17.81%) |
| occurrences (all) | 65 | 49 | 87 |
| PARAESTHESIA | | | |
| subjects affected / exposed | 44 / 394 (11.17%) | 37 / 400 (9.25%) | 53 / 393 (13.49%) |
| occurrences (all) | 50 | 42 | 59 |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| subjects affected / exposed | 54 / 394 (13.71%) | 58 / 400 (14.50%) | 65 / 393 (16.54%) |
| occurrences (all) | 59 | 65 | 73 |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 104 / 394 (26.40%) | 146 / 400 (36.50%) | 116 / 393 (29.52%) |
| occurrences (all) | 124 | 183 | 134 |
| LEUKOPENIA | | | |
| subjects affected / exposed | 14 / 394 (3.55%) | 20 / 400 (5.00%) | 14 / 393 (3.56%) |
| occurrences (all) | 17 | 35 | 20 |
| NEUTROPENIA | | | |
| subjects affected / exposed | 70 / 394 (17.77%) | 60 / 400 (15.00%) | 72 / 393 (18.32%) |
| occurrences (all) | 107 | 85 | 111 |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 45 / 394 (11.42%) | 49 / 400 (12.25%) | 53 / 393 (13.49%) |
| occurrences (all) | 64 | 78 | 74 |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 20 / 394 (5.08%) | 29 / 400 (7.25%) | 36 / 393 (9.16%) |
| occurrences (all) | 24 | 36 | 48 |
| DIARRHOEA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 98 / 394 (24.87%) | 82 / 400 (20.50%) | 125 / 393 (31.81%) |
| occurrences (all) | 133 | 137 | 221 |
| CONSTIPATION | | | |
| subjects affected / exposed | 92 / 394 (23.35%) | 103 / 400 (25.75%) | 122 / 393 (31.04%) |
| occurrences (all) | 115 | 128 | 151 |
| DRY MOUTH | | | |
| subjects affected / exposed | 6 / 394 (1.52%) | 13 / 400 (3.25%) | 20 / 393 (5.09%) |
| occurrences (all) | 6 | 16 | 22 |
| NAUSEA | | | |
| subjects affected / exposed | 124 / 394 (31.47%) | 130 / 400 (32.50%) | 149 / 393 (37.91%) |
| occurrences (all) | 177 | 210 | 223 |
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 9 / 394 (2.28%) | 11 / 400 (2.75%) | 20 / 393 (5.09%) |
| occurrences (all) | 11 | 13 | 20 |
| STOMATITIS | | | |
| subjects affected / exposed | 24 / 394 (6.09%) | 23 / 400 (5.75%) | 54 / 393 (13.74%) |
| occurrences (all) | 30 | 27 | 73 |
| VOMITING | | | |
| subjects affected / exposed | 67 / 394 (17.01%) | 69 / 400 (17.25%) | 71 / 393 (18.07%) |
| occurrences (all) | 105 | 92 | 99 |
| Skin and subcutaneous tissue disorders | | | |
| DRY SKIN | | | |
| subjects affected / exposed | 9 / 394 (2.28%) | 24 / 400 (6.00%) | 29 / 393 (7.38%) |
| occurrences (all) | 9 | 28 | 31 |
| ALOPECIA | | | |
| subjects affected / exposed | 180 / 394 (45.69%) | 180 / 400 (45.00%) | 188 / 393 (47.84%) |
| occurrences (all) | 183 | 182 | 195 |
| PRURITUS | | | |
| subjects affected / exposed | 25 / 394 (6.35%) | 52 / 400 (13.00%) | 58 / 393 (14.76%) |
| occurrences (all) | 29 | 72 | 76 |
| RASH | | | |
| subjects affected / exposed | 28 / 394 (7.11%) | 71 / 400 (17.75%) | 72 / 393 (18.32%) |
| occurrences (all) | 34 | 94 | 92 |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| PROTEINURIA | | | |
| subjects affected / exposed | 63 / 394 (15.99%) | 9 / 400 (2.25%) | 80 / 393 (20.36%) |
| occurrences (all) | 81 | 13 | 128 |
| Endocrine disorders | | | |
| HYPOTHYROIDISM | | | |
| subjects affected / exposed | 13 / 394 (3.30%) | 33 / 400 (8.25%) | 50 / 393 (12.72%) |
| occurrences (all) | 13 | 40 | 56 |
| Musculoskeletal and connective tissue disorders | | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 102 / 394 (25.89%) | 105 / 400 (26.25%) | 130 / 393 (33.08%) |
| occurrences (all) | 155 | 175 | 227 |
| BACK PAIN | | | |
| subjects affected / exposed | 43 / 394 (10.91%) | 51 / 400 (12.75%) | 57 / 393 (14.50%) |
| occurrences (all) | 50 | 70 | 67 |
| BONE PAIN | | | |
| subjects affected / exposed | 19 / 394 (4.82%) | 16 / 400 (4.00%) | 23 / 393 (5.85%) |
| occurrences (all) | 19 | 18 | 33 |
| MUSCLE SPASMS | | | |
| subjects affected / exposed | 7 / 394 (1.78%) | 10 / 400 (2.50%) | 20 / 393 (5.09%) |
| occurrences (all) | 8 | 10 | 24 |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 32 / 394 (8.12%) | 45 / 400 (11.25%) | 50 / 393 (12.72%) |
| occurrences (all) | 43 | 52 | 63 |
| MYALGIA | | | |
| subjects affected / exposed | 53 / 394 (13.45%) | 67 / 400 (16.75%) | 69 / 393 (17.56%) |
| occurrences (all) | 81 | 104 | 118 |
| Infections and infestations | | | |
| BRONCHITIS | | | |
| subjects affected / exposed | 16 / 394 (4.06%) | 15 / 400 (3.75%) | 28 / 393 (7.12%) |
| occurrences (all) | 17 | 16 | 37 |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 17 / 394 (4.31%) | 31 / 400 (7.75%) | 27 / 393 (6.87%) |
| occurrences (all) | 18 | 50 | 34 |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 16 / 394 (4.06%) | 24 / 400 (6.00%) | 37 / 393 (9.41%) |
| occurrences (all) | 20 | 43 | 56 |

| | | | |
|---|---|---|---|
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 28 / 394 (7.11%) | 37 / 400 (9.25%) | 35 / 393 (8.91%) |
| occurrences (all) | 37 | 51 | 57 |
| PNEUMONIA | | | |
| subjects affected / exposed | 15 / 394 (3.81%) | 21 / 400 (5.25%) | 19 / 393 (4.83%) |
| occurrences (all) | 17 | 23 | 22 |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 86 / 394 (21.83%) | 100 / 400 (25.00%) | 119 / 393 (30.28%) |
| occurrences (all) | 102 | 129 | 157 |
| DEHYDRATION | | | |
| subjects affected / exposed | 15 / 394 (3.81%) | 7 / 400 (1.75%) | 33 / 393 (8.40%) |
| occurrences (all) | 16 | 7 | 42 |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 16 / 394 (4.06%) | 24 / 400 (6.00%) | 36 / 393 (9.16%) |
| occurrences (all) | 18 | 30 | 47 |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 25 / 394 (6.35%) | 38 / 400 (9.50%) | 55 / 393 (13.99%) |
| occurrences (all) | 29 | 49 | 76 |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 17 / 394 (4.31%) | 13 / 400 (3.25%) | 23 / 393 (5.85%) |
| occurrences (all) | 20 | 14 | 32 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 21 November 2014 | Protocol was amended to change test product MPDL3280A to atezolizumab. |
| 31 May 2016 | Protocol was amended to include additional secondary end point to evaluate efficacy of atezolizumab as measured by investigator-assessed time to response (TTR) accordinto RECIST v1.1 for the ITT population, the TC1/2/3 or IC1/2/3 population, and the TC2/3 or IC2/3 population. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported