# Clinical trial results:
# A Phase III, Multicenter, Randomized, Open-Label Study Comparing Atezolizumab (Anti PD-L1 Antibody) in Combination With Adjuvant Anthracycline/Taxane-Based Chemotherapy Versus Chemotherapy Alone in Patients With Operable Triple Negative Breast Cancer

## Summary

| | |
|---|---|
| EudraCT number | 2016-003695-47 |
| Trial protocol | IE DE GB PL CZ ES HU DK AT BE IT RO |
| Global end of trial date | 14 August 2023 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 14 August 2024 |
| First version publication date | 14 August 2024 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | WO39391 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03498716 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Hoffmann-La Roche |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4058 |
| Public contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com |
| Scientific contact | Medical Communications, Hoffmann-La Roche, +41 616878333, global.trial_information@roche.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 18 August 2023 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 14 August 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

The objective of this trial was to evaluate the efficacy, safety, and pharmacokinetics of adjuvant atezolizumab in combination with paclitaxel, followed by atezolizumab, dose-dense doxorubicin or epirubicin (investigator's choice), and cyclophosphamide, compared with paclitaxel followed by dose-dense doxorubicin or epirubicin (investigator's choice) and cyclophosphamide alone in patients with Stage II-III triple negative breast cancer (TNBC).

Protection of trial subjects:

All study participants were required to read and sign an informed consent form (ICF).

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 02 August 2018 |
| 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: 17 |
| Country: Number of subjects enrolled | Australia: 27 |
| Country: Number of subjects enrolled | Austria: 10 |
| Country: Number of subjects enrolled | Belgium: 26 |
| Country: Number of subjects enrolled | Brazil: 58 |
| Country: Number of subjects enrolled | Switzerland: 8 |
| Country: Number of subjects enrolled | China: 268 |
| Country: Number of subjects enrolled | Czechia: 12 |
| Country: Number of subjects enrolled | Germany: 52 |
| Country: Number of subjects enrolled | Denmark: 22 |
| Country: Number of subjects enrolled | Spain: 75 |
| Country: Number of subjects enrolled | France: 143 |
| Country: Number of subjects enrolled | United Kingdom: 11 |
| Country: Number of subjects enrolled | Hong Kong: 14 |
| Country: Number of subjects enrolled | Hungary: 7 |
| Country: Number of subjects enrolled | Ireland: 17 |
| Country: Number of subjects enrolled | Israel: 12 |
| Country: Number of subjects enrolled | Italy: 73 |
| Country: Number of subjects enrolled | Japan: 249 |

| | |
|---|---|
| Country: Number of subjects enrolled | Korea, Republic of: 158 |
| Country: Number of subjects enrolled | Mexico: 74 |
| Country: Number of subjects enrolled | Peru: 10 |
| Country: Number of subjects enrolled | Poland: 14 |
| Country: Number of subjects enrolled | Romania: 21 |
| Country: Number of subjects enrolled | Russian Federation: 367 |
| Country: Number of subjects enrolled | Singapore: 3 |
| Country: Number of subjects enrolled | Thailand: 56 |
| Country: Number of subjects enrolled | Türkiye: 6 |
| Country: Number of subjects enrolled | Taiwan: 70 |
| Country: Number of subjects enrolled | Ukraine: 288 |
| Country: Number of subjects enrolled | United States: 31 |
| Worldwide total number of subjects | 2199 |
| EEA total number of subjects | 472 |

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) | 1821 |
| From 65 to 84 years | 376 |
| 85 years and over | 2 |

## Subject disposition

### Recruitment

Recruitment details:

Participants with newly diagnosed Stage II-III primary invasive Breast cancer (BC) that is of triple negative phenotype and who were to be treated with adjuvant systemic chemotherapy following definitive surgery, were enrolled in 342 centers in 31 countries.

### Pre-assignment

Screening details:

A total of 2199 participants were enrolled in the study. Participants were randomized in a 1:1 ratio to receive Atezolizumab and Chemotherapy or Chemotherapy alone.

### 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** | Chemotherapy |

Arm description:

Participants were administered paclitaxel, 80 milligram per square meter (mg/m^2), intravenous (IV) infusion weekly (QW) for maximum of 36 weeks followed by dose-dense doxorubicin, 60 mg/m^2 or dose-dense epirubicin, 90 mg/m^2 IV (investigator's choice) plus cyclophosphamide, 600 mg/m^2, IV repeated every 2 weeks (Q2W) for a maximum of 20 weeks supported with granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) treatment.

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

Dosage and administration details:

Paclitaxel 80 mg/m^2 QW IV infusion.

| | |
|---|---|
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Cyclophosphamide, 600 mg/m^2 Q2W IV infusion.

| | |
|---|---|
| Investigational medicinal product name | Epirubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Epirubicin 90 mg/m^2 IV infusion.

| | |
|---|---|
| Investigational medicinal product name | Doxorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |

| | |
|---|---|
| Routes of administration | Intravenous use |

Dosage and administration details:

Dxorubicin, 60 mg/m^2 IV infusion.

| **Arm title** | Atezolizumab and Chemotherapy |
|---|---|

Arm description:

Participants were administered atezolizumab 840 mg, IV infusion, Q2W in combination with chemotherapy (paclitaxel 80 mg/m^2, IV infusion QW for maximum of 22 weeks followed by dose-dense doxorubicin, 60 mg/m^2 or dose-dense epirubicin, 90 mg/m^2, IV (investigator's choice) plus cyclophosphamide, 600 mg/m^2, IV repeated Q2W for maximum of 17 weeks supported with G-CSF or GM-CSF treatment followed by atezolizumab, 1200 mg IV infusion every 3 weeks (Q3W) as a maintenance therapy to complete 1 year of atezolizumab treatment from the first dose.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Doxorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Dxorubicin, 60 mg/m^2 IV infusion.

| | |
|---|---|
| Investigational medicinal product name | Paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Paclitaxel 80 mg/m^2 QW IV infusion.

| | |
|---|---|
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Cyclophosphamide, 600 mg/m^2 Q2W IV infusion.

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

Dosage and administration details:

Atezolizumab 840 mg, Q2W and 1200 mg Q3W IV infusion.

| | |
|---|---|
| Investigational medicinal product name | Epirubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Epirubicin 90 mg/m^2 IV infusion.

| **Number of subjects in period 1** | Chemotherapy | Atezolizumab and Chemotherapy |
|---|---|---|
| Started | 1098 | 1101 |
| Safety Evaluable Population | 1084 | 1093 |
| Completed | 0 | 0 |
| Not completed | 1098 | 1101 |
| Adverse event, serious fatal | 58 | 72 |
| Consent withdrawn by subject | 88 | 73 |
| Physician decision | 4 | 2 |
| Disease Relapse | - | 1 |
| Study Terminated By Sponsor | 933 | 927 |
| Lost to follow-up | 15 | 26 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Chemotherapy |
| Reporting group description: | |
| Participants were administered paclitaxel, 80 milligram per square meter (mg/m^2), intravenous (IV) infusion weekly (QW) for maximum of 36 weeks followed by dose-dense doxorubicin, 60 mg/m^2 or dose-dense epirubicin, 90 mg/m^2 IV (investigator's choice) plus cyclophosphamide, 600 mg/m^2, IV repeated every 2 weeks (Q2W) for a maximum of 20 weeks supported with granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) treatment. | |
| Reporting group title | Atezolizumab and Chemotherapy |
| Reporting group description: | |
| Participants were administered atezolizumab 840 mg, IV infusion, Q2W in combination with chemotherapy (paclitaxel 80 mg/m^2, IV infusion QW for maximum of 22 weeks followed by dose-dense doxorubicin, 60 mg/m^2 or dose-dense epirubicin, 90 mg/m^2, IV (investigator's choice) plus cyclophosphamide, 600 mg/m^2, IV repeated Q2W for maximum of 17 weeks supported with G-CSF or GM-CSF treatment followed by atezolizumab, 1200 mg IV infusion every 3 weeks (Q3W) as a maintenance therapy to complete 1 year of atezolizumab treatment from the first dose. | |

| **Reporting group values** | Chemotherapy | Atezolizumab and Chemotherapy | Total |
|---|---|---|---|
| Number of subjects | 1098 | 1101 | 2199 |
| Age categorical<br>Units: Subjects | | | |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 52.8 | 52.3 | |
| standard deviation | ± 11.4 | ± 11.9 | - |
| Sex: Female, Male<br>Units: participants | | | |
| Female | 1094 | 1101 | 2195 |
| Male | 4 | 0 | 4 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 28 | 29 | 57 |
| Asian | 401 | 423 | 824 |
| Native Hawaiian or Other Pacific Islander | 1 | 0 | 1 |
| Black or African American | 2 | 8 | 10 |
| White | 567 | 554 | 1121 |
| More than one race | 0 | 1 | 1 |
| Unknown or Not Reported | 99 | 86 | 185 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 100 | 75 | 175 |
| Not Hispanic or Latino | 906 | 950 | 1856 |
| Unknown or Not Reported | 92 | 76 | 168 |

## End points

### End points reporting groups

| Reporting group title | Chemotherapy |
|---|---|

Reporting group description:

Participants were administered paclitaxel, 80 milligram per square meter (mg/m^2), intravenous (IV) infusion weekly (QW) for maximum of 36 weeks followed by dose-dense doxorubicin, 60 mg/m^2 or dose-dense epirubicin, 90 mg/m^2 IV (investigator's choice) plus cyclophosphamide, 600 mg/m^2, IV repeated every 2 weeks (Q2W) for a maximum of 20 weeks supported with granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) treatment.

| Reporting group title | Atezolizumab and Chemotherapy |
|---|---|

Reporting group description:

Participants were administered atezolizumab 840 mg, IV infusion, Q2W in combination with chemotherapy (paclitaxel 80 mg/m^2, IV infusion QW for maximum of 22 weeks followed by dose-dense doxorubicin, 60 mg/m^2 or dose-dense epirubicin, 90 mg/m^2, IV (investigator's choice) plus cyclophosphamide, 600 mg/m^2, IV repeated Q2W for maximum of 17 weeks supported with G-CSF or GM-CSF treatment followed by atezolizumab, 1200 mg IV infusion every 3 weeks (Q3W) as a maintenance therapy to complete 1 year of atezolizumab treatment from the first dose.

### Primary: Invasive Disease-Free Survival (iDFS)

| End point title | Invasive Disease-Free Survival (iDFS) |
|---|---|

End point description:

iDFS=time from randomization until date of first occurrence of 1 of the events: Ipsilateral invasive breast tumor recurrence (an invasive breast cancer involving same breast parenchyma as the original primary lesion); Ipsilateral local-regional invasive breast cancer recurrence (an invasive breast cancer in axilla, regional lymph nodes, chest wall, &/or skin of ipsilateral breast); Ipsilateral second primary invasive breast cancer; Contralateral invasive breast cancer; Distant recurrence (evidence of breast cancer in any anatomic site) that is histologically confirmed &/or clinically/radiographically diagnosed as recurrent invasive breast cancer; & Death attributable to any cause, including breast cancer, non-breast cancer, or unknown cause. Analysis using Kaplan-Meier estimates where participants with no events at time of analysis/no post-baseline data were censored. ITT population. 9999=Median & 95% CI were not estimable due to too few events having occurred.

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

End point timeframe:

From randomization until the occurrence of an iDFS event or death from any cause, whichever occurred earlier (up to 5 years)

| **End point values** | Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1098 | 1101 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9999 (9999 to 9999) | 9999 (9999 to 9999) | | |

## Statistical analyses

| Statistical analysis title | Chemotherapy Vs Atezolizumab and Chemotherapy |
|---|---|
| Comparison groups | Chemotherapy v Atezolizumab and Chemotherapy |
| Number of subjects included in analysis | 2199 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[1] |
| P-value | = 0.3846 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 1.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.87 |
| upper limit | 1.42 |

Notes:

[1] - Stratified Analysis: The stratification factors used in the analysis are axillary nodal status, surgery (breast conserving vs. mastectomy),and tumor PD-L1 status.

## Secondary: iDFS in the Subpopulation With Programmed Death-ligand 1 (PD-L1) Selected Tumor Status (IC1/2/3)

| End point title | iDFS in the Subpopulation With Programmed Death-ligand 1 (PD-L1) Selected Tumor Status (IC1/2/3) |
|---|---|

End point description:

iDFS=time from randomization until date of first occurrence of 1 of the events: Ipsilateral invasive breast tumor recurrence (an invasive breast cancer involving same breast parenchyma as the original primary lesion); Ipsilateral local-regional invasive breast cancer recurrence (an invasive breast cancer in axilla, regional lymph nodes, chest wall, &/or skin of ipsilateral breast); Ipsilateral second primary invasive breast cancer; Contralateral invasive breast cancer; Distant recurrence (evidence of breast cancer in any anatomic site) that is histologically confirmed &/or clinically/radiographically diagnosed as recurrent invasive breast cancer; & Death attributable to any cause, including breast cancer, non-breast cancer, or unknown cause. Analysis = Kaplan-Meier estimates where participants with no events at time of analysis/no post-baseline data were censored. PD-L1-positive subpopulation. 9999=Median & 95% CI were not estimable due to too few events having occurred.

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

End point timeframe:

From randomization until the occurrence of an iDFS event or death from any cause, whichever occurred earlier (up to 5 years)

| End point values | Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 782 | 785 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9999 (9999 to 9999) | 9999 (9999 to 9999) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: iDFS in the Node Positive Subpopulation

| End point title | iDFS in the Node Positive Subpopulation |
|---|---|

End point description:

iDFS=time from randomization until date of first occurrence of 1 of the events: Ipsilateral invasive breast tumor recurrence (an invasive breast cancer involving same breast parenchyma as the original primary lesion); Ipsilateral local-regional invasive breast cancer recurrence (an invasive breast cancer in axilla, regional lymph nodes, chest wall, &/or skin of ipsilateral breast); Ipsilateral second primary invasive breast cancer; Contralateral invasive breast cancer; Distant recurrence (evidence of breast cancer in any anatomic site) that is histologically confirmed &/or clinically/radiographically diagnosed as recurrent invasive breast cancer; & Death attributable to any cause, including breast cancer, non-breast cancer, or unknown cause. Analysis = Kaplan-Meier estimates where participants with no events at time of analysis/no post-baseline data were censored. Node positive subpopulation. 9999=Median & 95% CI were not estimable due to too few events having occurred.

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

End point timeframe:

From randomization until the occurrence of an iDFS event or death from any cause, whichever occurred earlier (up to 5 years)

| **End point values** | Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 533 | 534 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9999 (9999 to 9999) | 9999 (9999 to 9999) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: iDFS Including Second Primary Non-Breast Invasive Cancer

| End point title | iDFS Including Second Primary Non-Breast Invasive Cancer |
|---|---|

End point description:

iDFS=time from randomization until date of first occurrence of 1 of the events: Ipsilateral invasive breast tumor recurrence (an invasive breast cancer involving same breast parenchyma as original primary lesion); Ipsilateral local-regional invasive breast cancer recurrence (invasive breast cancer in axilla, regional lymph nodes, chest wall, &/or skin of ipsilateral breast); Ipsilateral 2nd primary invasive breast cancer; 2nd primary non-breast invasive cancer; Contralateral invasive breast cancer; Distant recurrence (evidence of breast cancer in any anatomic site) histologically confirmed &/or clinically/radiographically diagnosed as recurrent invasive breast cancer;Death attributable to any cause, including breast cancer, non-breast cancer/unknown cause. Analysis=Kaplan-Meier estimates where participants with no events at time of analysis/no post-baseline data were censored. ITT population. 9999=Median & 95% CI were not estimable due to too few events having occurred.

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

End point timeframe:

From randomization up to death from any cause (up to 5 years)

| End point values | Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1098 | 1101 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9999 (9999 to 9999) | 9999 (9999 to 9999) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Survival (OS)

| End point title | Overall Survival (OS) |
|---|---|

End point description:

OS is defined as the time from randomization to the date of death due to any cause. Analysis used Kaplan-Meier estimates where participants with no events at the time of analysis or no post-baseline information were censored. ITT population included all randomized participants, whether or not the assigned study treatment was received. 9999 = Median and 95%CI for OS were not estimable due to too few events having occurred.

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

End point timeframe:

From randomization up to death from any cause, up to 5 years

| End point values | Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1098 | 1101 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9999 (9999 to 9999) | 9999 (9999 to 9999) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Recurrence-Free Interval (RFI)

| End point title | Recurrence-Free Interval (RFI) |
|---|---|

End point description:

RFI was defined as the time from randomization to the first occurrence of any recurrence (local, regional [including invasive ipsilateral tumor and invasive locoregional tumor], or distant), as determined by investigators. Analysis used Kaplan-Meier estimates where participants with no events at the time of analysis, participants with no events who died, or participants with no post-baseline information were censored. ITT population included all randomized participants, whether or not the assigned study treatment was received. 9999=Median and 95%CI for RFI were not estimable due to too few events having occurred.

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

End point timeframe:

From randomization up to 5 years

| **End point values** | Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1098 | 1101 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9999 (9999 to 9999) | 9999 (9999 to 9999) | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Distant Recurrence-Free Interval (DRFI)**

| End point title | Distant Recurrence-Free Interval (DRFI) |
|---|---|

End point description:

DRFI was defined as the time from randomization to the distant breast cancer recurrence. Analysis used Kaplan-Meier estimates where participants with no events at the time of analysis, participants with no events who died, or participants with no post-baseline information were censored. ITT population included all randomized participants, whether or not the assigned study treatment was received. 9999=Median and 95%CI for DRFI were not estimable due to too few events having occurred.

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

End point timeframe:

From randomization up to 5 years

| **End point values** | Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1098 | 1101 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9999 (9999 to 9999) | 9999 (9999 to 9999) | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change from Baseline (CFB) in European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30)**

## Patient reported Function (Role functioning [Q6, Q7])

| End point title | Change from Baseline (CFB) in European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30) Patient reported Function (Role functioning [Q6, Q7]) |
|---|---|

End point description:

EORTC QLQ-C30=cancer specific health-related quality-of life (QoL) questionnaire. For role functioning scale, participant responses to 2 questions "Q6: Were you limited in doing either your work or daily activities" & "Q7: Were you limited in pursuing your hobbies or other leisure time activities" were scored on a 4-point scale (1=Not at All to 4=Very Much). Scores were linearly transformed on a scale of 0 to 100, with a low score indicating better functioning. Negative change from baseline indicated improvement. Patient-reported outcome (PRO)-evaluable populations = all randomized participants, whether or not assigned study treatment was received with baseline PRO assessment & at least one post-baseline PRO assessment in the EORTC QLQC30. Overall number analyzed = number of participants with data available for analyses. Number analyzed = number of participants with data available for analyses at the specified timepoint. 9999=standard deviation was not estimable for one participant.

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

End point timeframe:

Baseline (Cycle 1 Day 1), Day 1 of Cycles 4, 6, 8, 10, 12, 14 & 16; end of treatment/discontinuation (approximately at Day 351); Follow up: Months 3 to 48 (Total duration is up to 5 years) Cycles 1-5= 28 day cycles; Cycles 6-16: 21 day cycles

| **End point values** | Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1083 | 1088 | | |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n= 1083, 1088) | 87.26 (± 18.92) | 86.43 (± 19.66) | | |
| CFB: Cycle 4 Day 1 (n= 1025, 1040) | -10.88 (± 25.00) | -10.26 (± 24.87) | | |
| CFB: Cycle 6 Day 1 (n= 938, 924) | -17.31 (± 29.94) | -16.56 (± 29.18) | | |
| CFB: Cycle 8 Day 1 (n= 902, 881) | -4.58 (± 23.58) | -4.58 (± 24.31) | | |
| CFB: Cycle 10 Day 1 (n= 898, 851) | -3.77 (± 23.59) | -3.43 (± 22.77) | | |
| CFB: Cycle 12 Day 1 (n= 869, 806) | -1.53 (± 22.39) | -1.59 (± 23.05) | | |
| CFB: Cycle 14 Day 1 (n= 830, 736) | -1.02 (± 21.69) | -0.70 (± 20.61) | | |
| CFB: Cycle 16 Day 1 (n= 628, 489) | -1.09 (± 23.16) | -0.10 (± 21.77) | | |
| Drug Completion/Early Discontinuation(n=896,964) | -2.66 (± 23.48) | -4.37 (± 26.12) | | |
| CFB: Follow-up Month 3 (n= 845, 872) | -0.26 (± 22.62) | -0.40 (± 23.34) | | |
| CFB: Follow-up Month 6 (n= 815, 818) | 0.20 (± 24.08) | 0.02 (± 24.03) | | |
| CFB: Follow-up Month 9 (n= 758, 741) | -0.18 (± 23.52) | 0.47 (± 23.35) | | |
| CFB: Follow-up Month 12 (n= 677, 697) | 0.32 (± 22.42) | 1.22 (± 21.95) | | |
| CFB: Follow-up Month 18 (n= 528, 548) | -0.47 (± 24.41) | 1.52 (± 21.82) | | |
| CFB: Follow-up Month 24 (n= 374, 393) | 0.67 (± 23.54) | 1.74 (± 22.28) | | |

| | | | | |
|---|---|---|---|---|
| CFB: Follow-up Month 30 (n= 223, 249) | 2.24 (± 23.36) | 2.01 (± 24.19) | | |
| CFB: Follow-up Month 36 (n= 119, 130) | 3.08 (± 23.57) | 4.74 (± 20.36) | | |
| CFB: Follow-up Month 48 (n= 1, 5) | 0.00 (± 9999) | 13.33 (± 13.94) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Disease-Free Survival (DFS)

| End point title | Disease-Free Survival (DFS) |
|---|---|

End point description:

DFS was defined as the time from randomization to the first occurrence of disease recurrence or death from any cause. DFS events include: Ipsilateral invasive breast tumor recurrence; Ipsilateral local-regional invasive breast cancer recurrence; Distant recurrence that has either been histologically confirmed or clinically diagnosed as recurrent invasive breast cancer; Contralateral invasive breast cancer; Ipsilateral or contralateral DCIS; Second primary non-breast invasive cancer; Death attributable to any cause. Analysis using Kaplan-Meier estimates where participants with no events at the time of analysis or no post-baseline information were censored. ITT population included all randomized participants, whether or not the assigned study treatment was received. 9999=Median and 95%CI for DFS were not estimable due to too few events having occurred.

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

End point timeframe:

From randomization up to first disease recurrence or death from any cause (up to 5 years)

| **End point values** | Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1098 | 1101 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9999 (9999 to 9999) | 9999 (9999 to 9999) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in EORTC QLQ-C30 Patient-reported Function (Physical functioning [Q1-Q5])

| End point title | Change from Baseline in EORTC QLQ-C30 Patient-reported Function (Physical functioning [Q1-Q5]) |
|---|---|

End point description:

EORTC QLQ-C30 = cancer specific health-related quality-of life (QoL) questionnaire. For physical functioning scale, participant responses to 5 questions about daily activities (strenuous activities, long walks, short walks, bed/chair rest & needing help with eating, dressing, washing themselves, or using the toilet) were scored on a 4-point scale (1=Not at All to 4=Very Much). Scores were linearly transformed on a scale of 0 to 100, with a high score indicating worst functioning. Negative change from baseline = improvement in functioning. PRO-evaluable populations=all randomized participants, whether

or not the assigned study treatment was received with baseline PRO assessment and at least one post-baseline PRO assessment in the EORTC QLQC30. Overall number analyzed = number of participants with data available for analyses. Number analyzed=number of participants with data available for analyses at the specified timepoint. 9999=standard deviation was not estimable for one participant.

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

End point timeframe:

Baseline (Cycle 1 Day 1), Day 1 of Cycles 4, 6, 8, 10, 12, 14 & 16; end of treatment/discontinuation (approximately at Day 351); Follow up: Months 3 to 48 (Total duration is up to 5 years) Cycles 1-5= 28 day cycles; Cycles 6-16: 21 day cycles

| **End point values** | Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1083 | 1089 | | |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| CFB: Cycle 4 Day 1 (n=1025,1042) | -8.93 (± 14.97) | -8.69 (± 14.91) | | |
| CFB: Cycle 6 Day 1 (n=938, 925) | -13.30 (± 18.63) | -13.55 (± 18.47) | | |
| CFB: Cycle 8 Day 1 (n=901, 882) | -5.33 (± 13.79) | -6.42 (± 14.41) | | |
| CFB: Cycle 10 Day 1 (n=898, 852) | -3.71 (± 13.28) | -4.42 (± 13.15) | | |
| CFB: Cycle 12 Day 1 (n=871, 807) | -2.41 (± 12.87) | -3.42 (± 12.95) | | |
| CFB: Cycle 14 Day 1 (n=829, 736) | -1.41 (± 12.87) | -1.92 (± 12.11) | | |
| CFB: Cycle 16 Day 1 (n=627, 489) | -1.65 (± 12.78) | -1.82 (± 12.12) | | |
| Drug Completion/Early Discontinuation(n=895, 965) | -2.56 (± 13.72) | -4.68 (± 16.69) | | |
| CFB: Follow-up Month 3 (n=844, 871) | -1.62 (± 12.71) | -2.29 (± 13.47) | | |
| CFB: Follow-up Month 6 (n=815, 818) | -1.70 (± 13.46) | -1.96 (± 13.78) | | |
| CFB: Follow-up Month 9 (n=757, 741) | -1.55 (± 13.75) | -1.33 (± 13.91) | | |
| CFB: Follow-up Month 12 (n=676, 697) | -1.70 (± 13.85) | -1.37 (± 13.39) | | |
| CFB: Follow-up Month 18 (n=527, 548) | -1.92 (± 13.60) | -0.91 (± 13.79) | | |
| CFB: Follow-up Month 24 (n=374, 392) | -1.37 (± 13.89) | -0.72 (± 12.91) | | |
| Follow-up Month 30 (n=223, 249) | -1.61 (± 15.61) | -0.74 (± 12.72) | | |
| CFB: Follow-up Month 36 (n=119, 130) | -0.42 (± 14.40) | 0.82 (± 13.18) | | |
| CFB: Follow-up Month 48 (n=1, 5) | -13.33 (± 9999) | -2.67 (± 3.65) | | |
| Baseline (n=1083, 1089) | 89.86 (± 12.14) | 89.92 (± 11.57) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in EORTC QLQ-C30 Global Health Status (GHS) [Q29] and Health-Related Quality of Life (HRQoL) [Q30] Combined Score

| End point title | Change From Baseline in EORTC QLQ-C30 Global Health Status (GHS) [Q29] and Health-Related Quality of Life (HRQoL) [Q30] Combined Score |
|---|---|

End point description:

EORTC QLQ-C30=cancer specific health-related quality-of life (QoL) questionnaire. Participant responses to questions regarding GHS (Q29: "How would you rate your overall health during past week?") & QoL (Q30: "How would you rate your overall quality of life during the past week?") are scored on a 7-point scale (1= Very poor to 7=Excellent). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. Higher score = a better outcome. Negative change from Baseline values indicated deterioration in QOL or functioning and positive values indicated improvement. PRO-evaluable populations = participants in ITT population with baseline PRO assessment and at least one post-baseline PRO assessment in EORTC QLQC30. Overall number analyzed = number of participants with data available for analyses. Number analyzed = number of participants with data available for analysis at the specified time point. 9999=standard deviation was not estimable for 1 participant.

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

End point timeframe:

Baseline (Cycle 1 Day 1), Day 1 of Cycles 4, 6, 8, 10, 12, 14 & 16; end of treatment/discontinuation (approximately at Day 351); Follow up: Months 3 to 48 (Total duration is up to 5 years) Cycles 1-5= 28 day cycles; Cycles 6-16: 21 day cycles

| **End point values** | Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1081 | 1087 | | |
| Units: score on scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=1081, 1087) | 76.26 (± 18.15) | 75.90 (± 18.52) | | |
| CFB:Cycle 4 Day 1 (n=1022, 1040) | -10.49 (± 20.25) | -10.02 (± 19.48) | | |
| CFB:Cycle 6 Day 1 (n= 933, 924) | -15.87 (± 23.83) | -15.68 (± 22.32) | | |
| CFB:Cycle 8 Day 1 (n= 899, 881) | -3.54 (± 19.72) | -5.09 (± 18.88) | | |
| CFB:Cycle 10 Day 1(n= 893, 851) | -1.84 (± 19.57) | -2.82 (± 18.38) | | |
| CFB:Cycle 12 Day 1 (n= 869, 805) | -0.71 (± 19.41) | -2.31 (± 18.91) | | |
| CFB:Cycle 14 Day 1 (n= 828, 736) | -0.37 (± 19.04) | -1.25 (± 18.35) | | |
| CFB:Cycle 16 Day 1 (n= 627, 489) | 0.08 (± 18.56) | -1.30 (± 18.34) | | |
| Drug Completion/Early Discontinuation(n= 894, 962) | -1.56 (± 20.68) | -4.39 (± 22.01) | | |
| CFB: Follow-up Month 3 (n= 843, 871) | 1.01 (± 20.25) | -0.74 (± 20.50) | | |
| CFB: Follow-up Month 6 (n= 813, 815) | 1.10 (± 20.23) | -0.90 (± 20.72) | | |
| CFB: Follow-up Month 9 (n= 756, 740) | 0.62 (± 20.47) | 0.07 (± 20.83) | | |
| CFB: Follow-up Month 12 (n= 675, 697) | 1.21 (± 20.42) | 0.19 (± 19.84) | | |

| | | | | |
|---|---|---|---|---|
| CFB: Follow-up Month 18 (n= 526, 547) | 1.09 (± 22.18) | 0.47 (± 20.77) | | |
| CFB: Follow-up Month 24 (n= 373, 390) | 2.32 (± 22.30) | 0.43 (± 21.33) | | |
| CFB: Follow-up Month 30 (n= 222, 248) | 1.54 (± 21.36) | -0.57 (± 22.43) | | |
| CFB: Follow-up Month 36 (n= 117, 129) | 2.64 (± 20.95) | 0.58 (± 23.57) | | |
| CFB: Follow-up Month 48 (n=1, 4) | 0.00 (± 9999) | 6.25 (± 31.46) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants With Adverse Events

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

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product, regardless of causal attribution. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events. AEs are reported based on the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), Version 5.0. Safety Evaluable Population included all participants who received any amount of any study drug.

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

End point timeframe:

Up to 5 years

| **End point values** | Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1084 | 1093 | | |
| Units: participants | 1074 | 1090 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Serum Concentration of Atezolizumab

| End point title | Serum Concentration of Atezolizumab[2] |
|---|---|

End point description:

Pharmacokinetic (PK)-evaluable population included all participants who received any dose of study medication and who have at least one evaluable postbaseline PK sample. Overall number analyzed is the number of participants with data available for analyses. Number analyzed is the number of participants with data available for analysis at the specified time point. Number analyzed=number of participants with data available for analyses at the specified timepoint.

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

End point timeframe:

Postdose Day 1 of Cycle 1; Predose Day 1 of Cycles 2, 3, and 4; Predose Cycles 6, 10, and 14; Predose

Day 1 of Cycle 16;
Cycles 1-5= 28-day cycles; Cycles 6-16: 21-day cycles

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive statistic were planned to be analyzed for this end point.

| **End point values** | Atezolizumab and Chemotherapy | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 952 | | | |
| Units: microgram per milliliter (µg/mL) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Postdose Cycle 1 Day 1 (n=853) | 319 (± 43.3) | | | |
| Pre-dose: Cycle 2 Day 1 (n=854) | 153 (± 85.2) | | | |
| Pre-dose: Cycle 3 Day 1 (n=833) | 220 (± 62.0) | | | |
| Pre-dose: Cycle 4 Day 1 (n=819) | 221 (± 120.4) | | | |
| Pre-dose: Cycle 6 (n=727) | 239 (± 146.9) | | | |
| Pre-dose: Cycle 10 (n=650) | 250 (± 92.2) | | | |
| Pre-dose: Cycle 14 (n=556) | 258 (± 118.7) | | | |
| Pre-dose: Cycle 16 Day 2 (n=2) | 355 (± 29.5) | | | |

## Statistical analyses

No statistical analyses for this end point

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

| End point title | Percentage of Participants with Anti-Drug Antibodies (ADAs) to Atezolizumab[3] |
|---|---|

End point description:

Baseline evaluable participant= participant with an ADA assay result from a baseline sample(s). Post-baseline evaluable participant= participant with an ADA assay result from at least one postbaseline sample. Number analyzed at baseline and postbaseline are unique number of participants out of all the assessed participants who may have been ADA positive at that timepoint. Different participants may have contributed data for baseline and postbaseline. Safety Evaluable Population included all participants who received any amount of any study drug.

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

End point timeframe:

Up to 5 years

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive statistic were planned to be analyzed for this end point.

| End point values | Atezolizumab and Chemotherapy | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1093 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline (n=899) | 2.1 | | | |
| Post-baseline (n=901) | 11.5 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 5 years

Adverse event reporting additional description:

All-cause Mortality: ITT population population included all randomized participants, whether or not the assigned study treatment was received; Adverse Events: Safety Evaluable Population included all participants who received any amount of any study drug.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 26.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Chemotherapy |

Reporting group description:

Participants were administered paclitaxel, 80 mg/m^2, IV infusion QW for maximum of 36 weeks followed by dose-dense doxorubicin, 60 mg/m^2 or dose-dense epirubicin, 90 mg/m^2 IV (investigator's choice) plus cyclophosphamide, 600 mg/m^2, IV repeated Q2W for a maximum of 20 weeks supported with G-CSF or GM-CSF treatment.

| | |
|---|---|
| Reporting group title | Atezolizumab and Chemotherapy |

Reporting group description:

Participants were administered atezolizumab 840 mg, IV infusion, Q2W in combination with chemotherapy (paclitaxel 80 mg/m^2, IV infusion QW for maximum of 22 weeks followed by dose-dense doxorubicin, 60 mg/m^2 or dose-dense epirubicin, 90 mg/m^2, IV (investigator's choice) plus cyclophosphamide, 600 mg/m^2, IV repeated Q2W for maximum of 17 weeks supported with G-CSF or GM-CSF treatment followed by atezolizumab, 1200 mg IV infusion Q3W as a maintenance therapy to complete 1 year of atezolizumab treatment from the first dose.

| Serious adverse events | Chemotherapy | Atezolizumab and Chemotherapy | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 173 / 1084 (15.96%) | 280 / 1093 (25.62%) | |
| number of deaths (all causes) | 58 | 72 | |
| number of deaths resulting from adverse events | 1 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Thyroid cancer | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Benign neoplasm of thyroid gland | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Lobular breast carcinoma in situ | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Venous thrombosis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subclavian vein thrombosis | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jugular vein thrombosis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Deep vein thrombosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brachiocephalic vein thrombosis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Postoperative care | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cyst | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 3 / 1093 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 3 | |
| Device related thrombosis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Fatigue | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Implant site inflammation | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 4 / 1084 (0.37%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 4 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 10 / 1084 (0.92%) | 13 / 1093 (1.19%) | |
| occurrences causally related to treatment / all | 4 / 10 | 10 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 2 / 1084 (0.18%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Cytokine release syndrome | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sarcoidosis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Ovarian vein thrombosis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 1084 (0.37%) | 3 / 1093 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 4 / 1084 (0.37%) | 18 / 1093 (1.65%) | |
| occurrences causally related to treatment / all | 4 / 4 | 17 / 20 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 3 / 1084 (0.28%) | 6 / 1093 (0.55%) | |
| occurrences causally related to treatment / all | 3 / 3 | 6 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperventilation | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis chronic | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eosinophilic pneumonia | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression suicidal | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 14 / 1084 (1.29%) | 11 / 1093 (1.01%) | |
| occurrences causally related to treatment / all | 14 / 14 | 16 / 16 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 7 / 1093 (0.64%) | |
| occurrences causally related to treatment / all | 0 / 0 | 6 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gamma-glutamyltransferase | | | |

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|---|---|---|---|
| increased | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 2 / 1084 (0.18%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 1084 (0.18%) | 3 / 1093 (0.27%) | |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SARS-CoV-2 test positive | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 6 / 1084 (0.55%) | 10 / 1093 (0.91%) | |
| occurrences causally related to treatment / all | 6 / 6 | 13 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |

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|---|---|---|---|
| Foot fracture | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin laceration | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seroma | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 3 / 1093 (0.27%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius fracture | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post lumbar puncture syndrome | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic fracture | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infusion related reaction | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 1084 (0.00%) | 6 / 1093 (0.55%) | |
| occurrences causally related to treatment / all | 0 / 0 | 7 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immunisation reaction | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fracture | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Synovial rupture | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound complication | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular access site inflammation | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac asthma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Extrasystoles | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Myocarditis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1084 (0.00%) | 3 / 1093 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Encephalopathy | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Posterior reversible encephalopathy syndrome | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tremor | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Blood and lymphatic system disorders** | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 1084 (0.28%) | 6 / 1093 (0.55%) | |
| occurrences causally related to treatment / all | 3 / 3 | 4 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia macrocytic | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 23 / 1084 (2.12%) | 29 / 1093 (2.65%) | |
| occurrences causally related to treatment / all | 25 / 25 | 35 / 35 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Autoimmune haemolytic anaemia | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Granulocytopenia | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukopenia | | | |
| subjects affected / exposed | 5 / 1084 (0.46%) | 18 / 1093 (1.65%) | |
| occurrences causally related to treatment / all | 6 / 6 | 28 / 28 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphadenopathy mediastinal | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Methaemoglobinaemia | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelosuppression | | | |
| subjects affected / exposed | 3 / 1084 (0.28%) | 4 / 1093 (0.37%) | |
| occurrences causally related to treatment / all | 4 / 4 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 31 / 1084 (2.86%) | 40 / 1093 (3.66%) | |
| occurrences causally related to treatment / all | 41 / 41 | 76 / 76 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphopenia | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Deafness neurosensory | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal detachment | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 1084 (0.18%) | 3 / 1093 (0.27%) | |
| occurrences causally related to treatment / all | 2 / 2 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Colitis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 3 / 1093 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 3 / 1093 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal inflammation | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune-mediated enterocolitis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mesenteric artery thrombosis | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 2 / 1084 (0.18%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 3 / 3 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Proctitis | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatic failure | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Autoimmune hepatitis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis chronic | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic function abnormal | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 1084 (0.09%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 3 / 1093 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Photosensitivity reaction | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 4 / 1093 (0.37%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis noninfective | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tubulointerstitial nephritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Adrenocorticotropic hormone deficiency | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Addison's disease | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 6 / 1093 (0.55%) | |
| occurrences causally related to treatment / all | 0 / 0 | 6 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypopituitarism | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 4 / 1093 (0.37%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inappropriate antidiuretic hormone secretion | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypophysitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1084 (0.00%) | 3 / 1093 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma muscle | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft tissue disorder | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Torticollis | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Anal abscess | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast abscess | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cellulitis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopulmonary aspergillosis | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 7 / 1084 (0.65%) | 9 / 1093 (0.82%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| COVID-19 pneumonia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 1084 (0.18%) | 3 / 1093 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Cellulitis | | | |
| subjects affected / exposed | 2 / 1084 (0.18%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Complicated appendicitis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 2 / 1084 (0.18%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 2 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infected seroma | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Klebsiella infection | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphadenitis bacterial | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasopharyngitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Necrotising fasciitis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ophthalmic herpes zoster | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paronychia | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periorbital cellulitis | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 17 / 1084 (1.57%) | 18 / 1093 (1.65%) | |
| occurrences causally related to treatment / all | 8 / 17 | 13 / 18 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Pneumonia bacterial | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 2 / 1084 (0.18%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft tissue infection | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin infection | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 3 / 1093 (0.27%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 1084 (0.18%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tubo-ovarian abscess | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 4 / 1093 (0.37%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular device infection | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral rash | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 3 / 1084 (0.28%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 4 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 2 / 1093 (0.18%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Type 1 diabetes mellitus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 2 / 1084 (0.18%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 1084 (0.09%) | 0 / 1093 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertriglyceridaemia | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 1084 (0.00%) | 1 / 1093 (0.09%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Chemotherapy | Atezolizumab and Chemotherapy | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 1068 / 1084 (98.52%) | 1082 / 1093 (98.99%) | |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 50 / 1084 (4.61%) | 63 / 1093 (5.76%) | |
| occurrences (all) | 52 | 65 | |
| General disorders and administration | | | |

| | | | |
|---|---|---|---|
| site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 230 / 1084 (21.22%) | 234 / 1093 (21.41%) | |
| occurrences (all) | 373 | 455 | |
| Fatigue | | | |
| subjects affected / exposed | 268 / 1084 (24.72%) | 325 / 1093 (29.73%) | |
| occurrences (all) | 348 | 490 | |
| Malaise | | | |
| subjects affected / exposed | 73 / 1084 (6.73%) | 81 / 1093 (7.41%) | |
| occurrences (all) | 83 | 92 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 76 / 1084 (7.01%) | 73 / 1093 (6.68%) | |
| occurrences (all) | 84 | 83 | |
| Pyrexia | | | |
| subjects affected / exposed | 105 / 1084 (9.69%) | 160 / 1093 (14.64%) | |
| occurrences (all) | 126 | 211 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 79 / 1084 (7.29%) | 132 / 1093 (12.08%) | |
| occurrences (all) | 85 | 158 | |
| Dyspnoea | | | |
| subjects affected / exposed | 56 / 1084 (5.17%) | 84 / 1093 (7.69%) | |
| occurrences (all) | 64 | 105 | |
| Epistaxis | | | |
| subjects affected / exposed | 73 / 1084 (6.73%) | 56 / 1093 (5.12%) | |
| occurrences (all) | 92 | 63 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 116 / 1084 (10.70%) | 140 / 1093 (12.81%) | |
| occurrences (all) | 122 | 158 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 240 / 1084 (22.14%) | 296 / 1093 (27.08%) | |
| occurrences (all) | 319 | 457 | |
| Aspartate aminotransferase increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 159 / 1084 (14.67%) | 246 / 1093 (22.51%) | |
| occurrences (all) | 215 | 372 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 38 / 1084 (3.51%) | 61 / 1093 (5.58%) | |
| occurrences (all) | 43 | 92 | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 57 / 1084 (5.26%) | 51 / 1093 (4.67%) | |
| occurrences (all) | 106 | 67 | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 86 / 1084 (7.93%) | 113 / 1093 (10.34%) | |
| occurrences (all) | 162 | 214 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 254 / 1084 (23.43%) | 273 / 1093 (24.98%) | |
| occurrences (all) | 473 | 558 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 196 / 1084 (18.08%) | 232 / 1093 (21.23%) | |
| occurrences (all) | 392 | 526 | |
| Weight decreased | | | |
| subjects affected / exposed | 27 / 1084 (2.49%) | 63 / 1093 (5.76%) | |
| occurrences (all) | 30 | 67 | |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 70 / 1084 (6.46%) | 74 / 1093 (6.77%) | |
| occurrences (all) | 95 | 90 | |
| Radiation skin injury | | | |
| subjects affected / exposed | 13 / 1084 (1.20%) | 95 / 1093 (8.69%) | |
| occurrences (all) | 13 | 98 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 58 / 1084 (5.35%) | 71 / 1093 (6.50%) | |
| occurrences (all) | 68 | 104 | |
| Dysgeusia | | | |
| subjects affected / exposed | 117 / 1084 (10.79%) | 116 / 1093 (10.61%) | |
| occurrences (all) | 127 | 129 | |

| | | | |
|---|---|---|---|
| Headache | | | |
| subjects affected / exposed | 135 / 1084 (12.45%) | 176 / 1093 (16.10%) | |
| occurrences (all) | 178 | 284 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 94 / 1084 (8.67%) | 91 / 1093 (8.33%) | |
| occurrences (all) | 106 | 111 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 151 / 1084 (13.93%) | 158 / 1093 (14.46%) | |
| occurrences (all) | 179 | 181 | |
| Paraesthesia | | | |
| subjects affected / exposed | 75 / 1084 (6.92%) | 72 / 1093 (6.59%) | |
| occurrences (all) | 99 | 117 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 185 / 1084 (17.07%) | 196 / 1093 (17.93%) | |
| occurrences (all) | 193 | 207 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 422 / 1084 (38.93%) | 420 / 1093 (38.43%) | |
| occurrences (all) | 546 | 586 | |
| Neutropenia | | | |
| subjects affected / exposed | 240 / 1084 (22.14%) | 236 / 1093 (21.59%) | |
| occurrences (all) | 437 | 474 | |
| Leukopenia | | | |
| subjects affected / exposed | 139 / 1084 (12.82%) | 137 / 1093 (12.53%) | |
| occurrences (all) | 274 | 317 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 61 / 1084 (5.63%) | 72 / 1093 (6.59%) | |
| occurrences (all) | 73 | 79 | |
| Vomiting | | | |
| subjects affected / exposed | 146 / 1084 (13.47%) | 177 / 1093 (16.19%) | |
| occurrences (all) | 212 | 242 | |
| Stomatitis | | | |
| subjects affected / exposed | 120 / 1084 (11.07%) | 143 / 1093 (13.08%) | |
| occurrences (all) | 133 | 166 | |

| | | | |
|---|---|---|---|
| Nausea | | | |
| subjects affected / exposed | 531 / 1084 (48.99%) | 553 / 1093 (50.59%) | |
| occurrences (all) | 865 | 958 | |
| Dyspepsia | | | |
| subjects affected / exposed | 58 / 1084 (5.35%) | 65 / 1093 (5.95%) | |
| occurrences (all) | 73 | 71 | |
| Diarrhoea | | | |
| subjects affected / exposed | 188 / 1084 (17.34%) | 287 / 1093 (26.26%) | |
| occurrences (all) | 260 | 430 | |
| Constipation | | | |
| subjects affected / exposed | 210 / 1084 (19.37%) | 231 / 1093 (21.13%) | |
| occurrences (all) | 252 | 270 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 52 / 1084 (4.80%) | 79 / 1093 (7.23%) | |
| occurrences (all) | 53 | 92 | |
| Skin and subcutaneous tissue disorders | | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 41 / 1084 (3.78%) | 79 / 1093 (7.23%) | |
| occurrences (all) | 50 | 91 | |
| Rash | | | |
| subjects affected / exposed | 89 / 1084 (8.21%) | 167 / 1093 (15.28%) | |
| occurrences (all) | 110 | 200 | |
| Pruritus | | | |
| subjects affected / exposed | 50 / 1084 (4.61%) | 127 / 1093 (11.62%) | |
| occurrences (all) | 56 | 160 | |
| Nail discolouration | | | |
| subjects affected / exposed | 99 / 1084 (9.13%) | 106 / 1093 (9.70%) | |
| occurrences (all) | 108 | 113 | |
| Dry skin | | | |
| subjects affected / exposed | 36 / 1084 (3.32%) | 55 / 1093 (5.03%) | |
| occurrences (all) | 38 | 57 | |
| Alopecia | | | |
| subjects affected / exposed | 715 / 1084 (65.96%) | 735 / 1093 (67.25%) | |
| occurrences (all) | 733 | 752 | |
| Endocrine disorders | | | |

| | | | |
|---|---|---|---|
| Hypothyroidism | | | |
| subjects affected / exposed | 6 / 1084 (0.55%) | 161 / 1093 (14.73%) | |
| occurrences (all) | 6 | 173 | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 3 / 1084 (0.28%) | 62 / 1093 (5.67%) | |
| occurrences (all) | 3 | 65 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 73 / 1084 (6.73%) | 116 / 1093 (10.61%) | |
| occurrences (all) | 92 | 145 | |
| Arthralgia | | | |
| subjects affected / exposed | 150 / 1084 (13.84%) | 218 / 1093 (19.95%) | |
| occurrences (all) | 246 | 333 | |
| Bone pain | | | |
| subjects affected / exposed | 62 / 1084 (5.72%) | 68 / 1093 (6.22%) | |
| occurrences (all) | 72 | 79 | |
| Pain in extremity | | | |
| subjects affected / exposed | 50 / 1084 (4.61%) | 66 / 1093 (6.04%) | |
| occurrences (all) | 58 | 82 | |
| Myalgia | | | |
| subjects affected / exposed | 175 / 1084 (16.14%) | 202 / 1093 (18.48%) | |
| occurrences (all) | 309 | 347 | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 34 / 1084 (3.14%) | 71 / 1093 (6.50%) | |
| occurrences (all) | 34 | 72 | |
| Metabolism and nutrition disorders | | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 51 / 1084 (4.70%) | 73 / 1093 (6.68%) | |
| occurrences (all) | 64 | 89 | |
| Decreased appetite | | | |
| subjects affected / exposed | 144 / 1084 (13.28%) | 213 / 1093 (19.49%) | |
| occurrences (all) | 185 | 275 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 02 November 2017 | Protocol Amendment 1: The guidelines for managing patients who experienced atezolizumab-associated adverse events were revised to include guidelines for hypophysitis and myocarditis. The interval for the periodic safety iDMC reviews was established to occur on a 6-month basis. |
| 20 May 2018 | Protocol Amendment 2: The study design was modified to align with recommendations by European Health authorities, including clarifying the secondary efficacy endpoint related to recurrence-free interval and some eligibility criteria. |
| 15 November 2018 | Protocol Amendment 3: The protocol was amended primarily to update safety information, including risks for atezolizumab and management guidelines, eligibility criteria, and changes to the adverse event severity grading scale. |
| 12 November 2019 | Protocol Amendment 4: Safety information was updated and recommendations implemented in response to Health Authority request. |
| 14 February 2020 | Protocol Amendment 5: The protocol converged country-specific criteria into the global amendment. In addition, requirements for membership in the iDMC were clarified. Additional safety-related updates were also added. |
| 17 February 2021 | Protocol Amendment 6: The protocol was amended to update the risks and management guidelines for atezolizumab to align with the latest Atezolizumab Investigator's Brochure (Version 17). |
| 24 November 2021 | Protocol Amendment 7: The interim analysis timeline was updated and the adverse event management guidelines were revised to align with the latest Atezolizumab Investigator's Brochure (Version 18). |
| 01 March 2023 | Protocol Amendment 8: A formal efficacy and futility analysis was added due to FDA request to determine the ability of the study to provide an acceptable benefit-risk assessment upon trial conclusion. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported