# Clinical trial results:
# A Phase III Randomized Study to Investigate the Efficacy and Safety of Atezolizumab (Anti-PD-L1 Antibody) in Combination With Neoadjuvant Anthracycline/Nab-Paclitaxel-Based Chemotherapy Compared With Placebo and Chemotherapy in Patients With Primary Invasive Triple-Negative Breast Cancer

## Summary

| | |
|---|---|
| EudraCT number | 2016-004734-22 |
| Trial protocol | DE GB BE PL ES IT |
| Global end of trial date | 28 September 2022 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 14 October 2023 |
| First version publication date | 14 April 2021 |
| Version creation reason | |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | WO39392 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03197935 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Other Sponsor ID: IMpassion031 |

Notes:

**Sponsors**

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

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 28 September 2022 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 28 September 2022 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The main objectives of this study were to evaluate the efficacy, safety, and pharmacokinetics of neoadjuvant nab-paclitaxel and atezolizumab followed by doxorubicin and cyclophosphamide with atezolizumab or neoadjuvant nab-paclitaxel and placebo followed by doxorubicin and cyclophosphamide with placebo in participants with T2-4d triple-negative breast cancer (TNBC).

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 24 July 2017 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Safety |
| Long term follow-up duration | 49 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Australia: 4 |
| Country: Number of subjects enrolled | Belgium: 15 |
| Country: Number of subjects enrolled | Brazil: 113 |
| Country: Number of subjects enrolled | Canada: 11 |
| Country: Number of subjects enrolled | Germany: 48 |
| Country: Number of subjects enrolled | Spain: 4 |
| Country: Number of subjects enrolled | United Kingdom: 6 |
| Country: Number of subjects enrolled | Italy: 2 |
| Country: Number of subjects enrolled | Japan: 36 |
| Country: Number of subjects enrolled | Korea, Republic of: 27 |
| Country: Number of subjects enrolled | Poland: 5 |
| Country: Number of subjects enrolled | Taiwan: 21 |
| Country: Number of subjects enrolled | United States: 41 |
| Worldwide total number of subjects | 333 |
| EEA total number of subjects | 74 |

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) | 287 |
| From 65 to 84 years | 46 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Participants with clinically assessed T2-4d early or primary invasive triple-negative breast cancer (TNBC) who were eligible for surgery were included in the study.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo and Chemotherapy |

Arm description:

Participants received placebo matched to atezolizumab via IV infusion every 2 weeks in combination with nab-paclitaxel (125 mg/m^2) via IV infusion every week for 12 weeks, followed by placebo matched to atezolizumab every 2 weeks in combination with doxorubicin (60 mg/m^2) and cyclophosphamide (600 mg/m^2) every 2 weeks via IV infusions with filgrastim/pegfilgrastim support for 4 doses. Participants will continue to be followed after surgery.

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

Dosage and administration details:

Placebo matched to atezolizumab was administered intravenously every 2 weeks for 20 weeks.

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

Dosage and administration details:

Cyclophosphamide was administered after completion or early discontinuation of nab-paclitaxel at a dose of 600 mg/m^2 every 2 weeks intravenously for 4 doses.

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

Dosage and administration details:

Doxorubicin was administered after completion or early discontinuation of nab-paclitaxel at a dose of 60 mg/m^2 every 2 weeks intravenously for 4 doses.

| | |
|---|---|
| Investigational medicinal product name | Nab-paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |

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

Dosage and administration details:

Nab-paclitaxel was administered at a dose of 125 milligrams per square meter [mg/m^2] intravenously every week for 12 weeks.

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

Arm description:

Participants received atezolizumab (840 milligrams [mg]) via intravenous (IV) infusion every 2 weeks in combination with nab-paclitaxel (125 milligrams per square meter [mg/m^2]) via IV infusion every week for 12 weeks, followed by atezolizumab (840 mg) every 2 weeks in combination with doxorubicin (60 mg/m^2) and cyclophosphamide (600 mg/m^2) every 2 weeks via IV infusions with filgrastim/pegfilgrastim support for 4 doses. Participants continued to receive unblinded atezolizumab post-surgery at a fixed dose of 1200 mg by IV infusion every 3 weeks for 11 doses, for a total of approximately 12 months of atezolizumab therapy.

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

Dosage and administration details:

Atezolizumab was administered intravenously at a dose of 840 milligrams every 2 weeks for 20 weeks. Participants continued to receive unblinded atezolizumab post-surgery at a fixed dose of 1200 mg intravenously every 3 weeks for 11 doses, for a total of approximately 12 months of atezolizumab therapy.

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

Dosage and administration details:

Cyclophosphamide was administered after completion or early discontinuation of nab-paclitaxel at a dose of 600 mg/m^2 every 2 weeks intravenously for 4 doses.

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

Dosage and administration details:

Doxorubicin was administered after completion or early discontinuation of nab-paclitaxel at a dose of 60 mg/m^2 every 2 weeks intravenously for 4 doses.

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

Dosage and administration details:

Nab-paclitaxel was administered at a dose of 125 milligrams per square meter [mg/m^2] intravenously every week for 12 weeks.

| **Number of subjects in period 1** | Placebo and Chemotherapy | Atezolizumab and Chemotherapy |
|---|---|---|
| Started | 168 | 165 |
| Completed | 121 | 136 |
| Not completed | 47 | 29 |
| Physician decision | 2 | 1 |
| Consent withdrawn by subject | 16 | 8 |
| Death due to any cause | 26 | 15 |
| Lost to follow-up | 3 | 5 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo and Chemotherapy |
| Reporting group description: | |
| Participants received placebo matched to atezolizumab via IV infusion every 2 weeks in combination with nab-paclitaxel (125 mg/m^2) via IV infusion every week for 12 weeks, followed by placebo matched to atezolizumab every 2 weeks in combination with doxorubicin (60 mg/m^2) and cyclophosphamide (600 mg/m^2) every 2 weeks via IV infusions with filgrastim/pegfilgrastim support for 4 doses. Participants will continue to be followed after surgery. | |
| Reporting group title | Atezolizumab and Chemotherapy |
| Reporting group description: | |
| Participants received atezolizumab (840 milligrams [mg]) via intravenous (IV) infusion every 2 weeks in combination with nab-paclitaxel (125 milligrams per square meter [mg/m^2]) via IV infusion every week for 12 weeks, followed by atezolizumab (840 mg) every 2 weeks in combination with doxorubicin (60 mg/m^2) and cyclophosphamide (600 mg/m^2) every 2 weeks via IV infusions with filgrastim/pegfilgrastim support for 4 doses. Participants continued to receive unblinded atezolizumab post-surgery at a fixed dose of 1200 mg by IV infusion every 3 weeks for 11 doses, for a total of approximately 12 months of atezolizumab therapy. | |

| Reporting group values | Placebo and Chemotherapy | Atezolizumab and Chemotherapy | Total |
|---|---|---|---|
| Number of subjects | 168 | 165 | 333 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 139 | 148 | 287 |
| From 65-84 years | 29 | 17 | 46 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 50.3 | 50.1 | |
| standard deviation | ± 13.2 | ± 11.6 | - |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 168 | 165 | 333 |
| Male | 0 | 0 | 0 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 41 | 47 | 88 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 15 | 9 | 24 |
| White | 108 | 102 | 210 |
| More than one race | 0 | 4 | 4 |

| | | | |
|---|---|---|---|
| Unknown or Not Reported | 4 | 3 | 7 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 47 | 45 | 92 |
| Not Hispanic or Latino | 114 | 114 | 228 |
| Unknown or Not Reported | 7 | 6 | 13 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo and Chemotherapy |

Reporting group description:

Participants received placebo matched to atezolizumab via IV infusion every 2 weeks in combination with nab-paclitaxel (125 mg/m^2) via IV infusion every week for 12 weeks, followed by placebo matched to atezolizumab every 2 weeks in combination with doxorubicin (60 mg/m^2) and cyclophosphamide (600 mg/m^2) every 2 weeks via IV infusions with filgrastim/pegfilgrastim support for 4 doses. Participants will continue to be followed after surgery.

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

Reporting group description:

Participants received atezolizumab (840 milligrams [mg]) via intravenous (IV) infusion every 2 weeks in combination with nab-paclitaxel (125 milligrams per square meter [mg/m^2]) via IV infusion every week for 12 weeks, followed by atezolizumab (840 mg) every 2 weeks in combination with doxorubicin (60 mg/m^2) and cyclophosphamide (600 mg/m^2) every 2 weeks via IV infusions with filgrastim/pegfilgrastim support for 4 doses. Participants continued to receive unblinded atezolizumab post-surgery at a fixed dose of 1200 mg by IV infusion every 3 weeks for 11 doses, for a total of approximately 12 months of atezolizumab therapy.

### Primary: Number of Participants with Pathologic Complete Response (pCR) Using American Joint Committee on Cancer (AJCC) Staging System in ITT Population

| | |
|---|---|
| End point title | Number of Participants with Pathologic Complete Response (pCR) Using American Joint Committee on Cancer (AJCC) Staging System in ITT Population |

End point description:

Number of participants with Pathologic Complete Response (pCR) Using American Joint Committee on Cancer (AJCC) Staging System in ITT Population. pCR is defined as eradication of invasive tumor from both breast and lymph nodes (ypT0/is ypN0). pCR was evaluated for each participant after neoadjuvant study treatment and surgery. Participants whose pCR assessment was missing will be counted as not achieving a pCR.

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

End point timeframe:

After neoadjuvant study treatment and surgery, up to primary analysis data cut off on 03 April 2020.

| End point values | Placebo and Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 168 | 165 | | |
| Units: Number of Participants | 69 | 95 | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | pCR ITT Statistical Analysis |

Statistical analysis description:

Stratified analysis. Strata are: tumor PD-L1 status (IC0 vs. IC1/2/3) and clinical stage at presentation (Stage II vs. III).

| | |
|---|---|
| Comparison groups | Atezolizumab and Chemotherapy v Placebo and Chemotherapy |

| | |
|---|---|
| Number of subjects included in analysis | 333 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0044 [1] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Absolute difference in pCR |
| Point estimate | 16.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 5.91 |
| upper limit | 27.1 |

Notes:

[1] - (one-sided)

## Primary: Number of Participants with pCR in Subpopulation with PD-L1-Positive Tumor Status (tumor-infiltrating immune cell [IC] 1/2/3) Using AJCC Staging System

| | |
|---|---|
| End point title | Number of Participants with pCR in Subpopulation with PD-L1-Positive Tumor Status (tumor-infiltrating immune cell [IC] 1/2/3) Using AJCC Staging System |

End point description:

Number of participants with Pathologic Complete Response (pCR) Using American Joint Committee on Cancer (AJCC) Staging System in the subpopulation with programmed death-ligand1 (PD-L1)-positive tumor status(tumor-infiltrating immune cell [IC] IC1/2/3) . pCR is defined as eradication of invasive tumor from both breast and lymph nodes (ypT0/is ypN0). pCR was evaluated for each participant after neoadjuvant study treatment and surgery. Participants whose pCR assessment was missing will be counted as not achieving a pCR.

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

End point timeframe:

After neoadjuvant study treatment and surgery, up to primary analysis data cut off on 03 April 2020.

| End point values | Placebo and Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 77 | | |
| Units: Number of Participants | 37 | 53 | | |

## Statistical analyses

| Statistical analysis title | pCR PD-L1-Positive Statistical Analysis |
|---|---|

Statistical analysis description:

Stratified analysis. Strata are: AJCC stage at diagnosis (II vs. III).

| | |
|---|---|
| Comparison groups | Placebo and Chemotherapy v Atezolizumab and Chemotherapy |

| | |
|---|---|
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0206 [2] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in pCR |
| Point estimate | 19.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.17 |
| upper limit | 34.83 |

Notes:

[2] - (one-sided)

## Secondary: Event-Free Survival (EFS) in All Participants

| | |
|---|---|
| End point title | Event-Free Survival (EFS) in All Participants |

End point description:

Event-free survival (EFS) defined as the time from randomization to the first documented occurrence of disease recurrence, disease progression, or death from any cause in all participants. Recurrent disease includes local, regional, or distant recurrence and contralateral breast cancer. Ipsilateral or contralateral in situ disease and second primary non-breast cancers (including in situ carcinomas and non-melanoma skin cancers) will not be counted as progressive disease or recurrent disease. Note: 999999=not estimable.

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

End point timeframe:

From randomization and up to study final analysis data cut off on 28 September 2022.

| End point values | Placebo and Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 168 | 165 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 999999 (999999 to 999999) | 999999 (999999 to 999999) | | |

### Statistical analyses

| Statistical analysis title | EFS All Participants Statistical Analysis |
|---|---|

Statistical analysis description:

Stratified analysis. Strata are: Tumor PD-L1 status (IC0 vs IC1/2/3) and AJCC stage at diagnosis (II vs. III).

| | |
|---|---|
| Comparison groups | Placebo and Chemotherapy v Atezolizumab and Chemotherapy |

| | |
|---|---|
| Number of subjects included in analysis | 333 |
| Analysis specification | Pre-specified |
| Analysis type | other[3] |
| Method | Stratified log-rank test |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.47 |
| upper limit | 1.21 |

Notes:

[3] - This study was not designed nor formally powered to demonstrate statistically significant improvements in the secondary efficacy endpoint of EFS. The analyses of this secondary endpoint are descriptive in nature.

## Secondary: Event-Free Survival (EFS) in Subpopulation with PD-L1-Postive Tumor Status

| | |
|---|---|
| End point title | Event-Free Survival (EFS) in Subpopulation with PD-L1-Postive Tumor Status |

End point description:

Event-free survival (EFS) defined as the time from randomization to the first documented occurrence of disease recurrence, disease progression, or death from any cause in the subpopulation with PD-L1-positive tumor status. Recurrent disease includes local, regional, or distant recurrence and contralateral breast cancer. Ipsilateral or contralateral in situ disease and second primary non-breast cancers (including in situ carcinomas and non-melanoma skin cancers) will not be counted as progressive disease or recurrent disease. Note: 999999=not estimable.

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

End point timeframe:

From randomization and up to study final analysis data cut off on 28 September 2022.

| **End point values** | Placebo and Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 77 | | |
| Units: Months | | | | |
| number (confidence interval 95%) | 999999 (999999 to 999999) | 999999 (999999 to 999999) | | |

## Statistical analyses

| **Statistical analysis title** | EFS Subpopulation With PD-L1-Positive Tumor Status |
|---|---|

Statistical analysis description:

Stratified analysis. Strata are: AJCC stage at diagnosis (II vs. III).

| | |
|---|---|
| Comparison groups | Placebo and Chemotherapy v Atezolizumab and Chemotherapy |

| | |
|---|---|
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | other[4] |
| Method | Stratified log-rank test |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.55 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.26 |
| upper limit | 1.18 |

Notes:

[4] - This study was not designed nor formally powered to demonstrate statistically significant improvements in the secondary efficacy endpoint of EFS. The analyses of this secondary endpoint are descriptive in nature.

## Secondary: Disease-Free Survival (DFS) in Subpopulation of Participants with PD-L1-Positive Tumor Status Who Undergo Surgery

| | |
|---|---|
| End point title | Disease-Free Survival (DFS) in Subpopulation of Participants with PD-L1-Positive Tumor Status Who Undergo Surgery |

End point description:

Disease-free survival (DFS) defined as the time from surgery to the first documented disease recurrence or death from any cause, whichever occurs first. DFS is analyzed with the use of the same methodology as specified for EFS for the subpopulation of participants with PD-L1-positive tumor status. Note: 999999=not estimable.

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

End point timeframe:

From surgery and up to study final analysis data cut off on 28 September 2022.

| **End point values** | Placebo and Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 67 | 73 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 999999 (999999 to 999999) | 999999 (999999 to 999999) | | |

## Statistical analyses

| **Statistical analysis title** | DFS PD-L1-Positive Tumor Status |
|---|---|

Statistical analysis description:

Stratified analysis. Strata are: AJCC stage at diagnosis (II vs. III).

| | |
|---|---|
| Comparison groups | Placebo and Chemotherapy v Atezolizumab and Chemotherapy |

| | |
|---|---|
| Number of subjects included in analysis | 140 |
| Analysis specification | Pre-specified |
| Analysis type | other[5] |
| Method | Stratified log-rank test |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.23 |
| upper limit | 1.43 |

Notes:

[5] - This study was not designed nor formally powered to demonstrate statistically significant improvements in the secondary efficacy endpoint of DFS. The analyses of this secondary endpoint are descriptive in nature.

## Secondary: Disease-Free Survival (DFS) in All Participants Who Undergo Surgery

| | |
|---|---|
| End point title | Disease-Free Survival (DFS) in All Participants Who Undergo Surgery |

End point description:

Disease-free survival (DFS) defined as the time from surgery to the first documented disease recurrence or death from any cause, whichever occurs first. DFS is analyzed with the use of the same methodology as specified for EFS for all participants. Note: 999999=not estimable.

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

End point timeframe:

From surgery and up to study final analysis data cut off on 28 September 2022.

| **End point values** | Placebo and Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 153 | 155 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 999999 (999999 to 999999) | 999999 (999999 to 999999) | | |

## Statistical analyses

| **Statistical analysis title** | DFS ITT Statistical Analysis |
|---|---|

Statistical analysis description:

Stratified analysis. Strata are: Tumor PD-L1 status (IC0 vs IC1/2/3) and AJCC stage at diagnosis (II vs. III).

| | |
|---|---|
| Comparison groups | Placebo and Chemotherapy v Atezolizumab and Chemotherapy |

| | |
|---|---|
| Number of subjects included in analysis | 308 |
| Analysis specification | Pre-specified |
| Analysis type | other[6] |
| Method | Stratified log-rank test |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.44 |
| upper limit | 1.3 |

Notes:

[6] - This study was not designed nor formally powered to demonstrate statistically significant improvements in the secondary efficacy endpoint of DFS. The analyses of this secondary endpoint are descriptive in nature.

## Secondary: Mean Scores for Function (Role/Physical) and GHS/HRQoL by Cycle and Between Treatment Arms as Assessed by the EORTC QLQ-C30

| | |
|---|---|
| End point title | Mean Scores for Function (Role/Physical) and GHS/HRQoL by Cycle and Between Treatment Arms as Assessed by the EORTC QLQ-C30 |

End point description:

Mean score in function (role, physical) and global health status(GHS)/ health-related quality of life (HRQoL) by cycle and between treatment arms as assessed by the functional and HRQoL scales of the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core30(QLQ C30). The score range for each scale and single-item measure is 0 to 100, where higher scores indicate a higher response level (i.e., better functioning, better QoL). Analysis population included all randomized participants with non-missing baseline assessment and at least one non-missing post-baseline assessment. Note: SDC=Study Drug Completion, ED=Early Discontinuation, SFU=Survival Follow-Up.

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

End point timeframe:

From randomization and up to study final analysis data cut off on 28 September 2022.

| **End point values** | Placebo and Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 167 | 161 | | |
| Units: Score on a 0-100 scale | | | | |
| arithmetic mean (confidence interval 95%) | | | | |
| GHS/QoL Baseline (n=167, 161) | 76.45 (73.47 to 79.42) | 79.24 (76.34 to 82.14) | | |
| GHS/QoL Cycle 2 Day 1 (n=164, 157) | 71.90 (69.04 to 74.76) | 71.55 (68.53 to 74.57) | | |
| GHS/QoL Cycle 3 Day 1 (n=152, 143) | 65.30 (62.25 to 68.34) | 62.65 (58.94 to 66.36) | | |
| GHS/QoL Cycle 4 Day 1 (n=153, 149) | 62.36 (59.15 to 65.58) | 59.84 (56.62 to 63.07) | | |
| GHS/QoL Cycle Cycle 5 Day 1 (n=147, 139) | 60.37 (56.87 to 63.87) | 53.60 (49.71 to 57.48) | | |
| GHS/QoL Cycle 6 Day 1 (n=134, 132) | 74.25 (70.86 to 77.65) | 70.14 (66.97 to 73.31) | | |
| GHS/QoL Cycle 7 Day 1 (n=122, 128) | 76.50 (73.39 to 79.62) | 73.57 (70.92 to 76.22) | | |

| | | | | |
|---|---|---|---|---|
| GHS/QoL Cycle 8 Day 1 (n=119, 122) | 77.17 (74.35 to 79.99) | 72.06 (69.01 to 75.11) | | |
| GHS/QoL Cycle 9 Day 1 (n=121, 121) | 75.62 (72.54 to 78.69) | 72.18 (69.18 to 75.17) | | |
| GHS/QoL Cycle 10 Day 1 (n=114, 122) | 75.22 (72.22 to 78.22) | 70.56 (67.09 to 74.03) | | |
| GHS/QoL Cycle 11 Day 1 (n=119, 122) | 75.98 (73.17 to 78.79) | 71.93 (68.53 to 75.32) | | |
| GHS/QoL Cycle 12 Day 1 (n=119, 122) | 75.84 (72.93 to 78.75) | 72.40 (69.27 to 75.54) | | |
| GHS/QoL Cycle 13 Day 1 (n=119, 121) | 74.72 (71.35 to 78.08) | 72.87 (69.67 to 76.06) | | |
| GHS/QoL Cycle 14 Day 1 (n=119, 116) | 74.79 (71.61 to 77.97) | 71.19 (67.65 to 74.43) | | |
| GHS/QoL Cycle 15 Day 1 (n=112, 116) | 75.00 (71.85 to 78.15) | 74.07 (71.08 to 77.06) | | |
| GHS/QoL Cycle 16 Day 1 (n=111, 114) | 77.70 (74.70 to 80.71) | 74.93 (71.69 to 78.16) | | |
| GHS/QoL SDC/ED (n=130, 137) | 75.38 (72.18 to 78.59) | 72.51 (68.96 to 76.05) | | |
| GHS/QoL SFU Month 3 (n=131, 142) | 76.97 (73.87 to 80.07) | 72.65 (69.33 to 75.98) | | |
| GHS/QoL SFU Month 6 (n=125, 136) | 74.93 (71.28 to 78.59) | 75.61 (72.09 to 79.14) | | |
| GHS/QoL SFU Month 9 (n=116, 132) | 75.00 (71.32 to 76.68) | 75.19 (71.78 to 78.60) | | |
| GHS/QoL SFU Month 12 (n=111, 126) | 75.15 (71.66 to 78.64) | 74.87 (71.13 to 78.60) | | |
| GHS/QoL SFU Month 18 (n=102, 112) | 76.39 (72.29 to 80.48) | 75.60 (72.01 to 79.18) | | |
| GHS/QoL SFU Month 24 (n=83, 108) | 78.31 (74.89 to 81.73) | 74.46 (70.55 to 78.37) | | |
| GHS/QoL SFU Month 30 (n=65, 72) | 78.33 (74.08 to 82.59) | 73.50 (68.56 to 78.43) | | |
| GHS/QoL SFU Month 36 (n=62, 69) | 78.63 (74.53 to 82.73) | 76.93 (71.85 to 82.01) | | |
| GHS/QoL SFU Month 48 (n=2, 7) | 58.33 (-259.32 to 375.99) | 63.10 (47.77 to 78.42) | | |
| Physical Functioning Baseline (n=166, 161) | 90.03 (87.82 to 92.24) | 90.85 (88.53 to 93.17) | | |
| Physical Functioning Cycle 2 Day 1 (n=164, 157) | 83.50 (80.79 to 86.21) | 84.93 (82.55 to 87.31) | | |
| Physical Functioning Cycle 3 Day 1 (n=152, 142) | 78.33 (75.19 to 81.48) | 77.29 (74.04 to 80.54) | | |
| Physical Functioning Cycle 4 Day 1 (n=152, 149) | 70.42 (67.06 to 73.77) | 69.02 (65.52 to 72.51) | | |
| Physical Functioning Cycle 5 Day 1 (n=146, 139) | 67.91 (64.18 to 71.65) | 64.27 (60.40 to 68.13) | | |
| Physical Functioning Cycle 6 Day 1 (n=134, 132) | 79.49 (76.38 to 82.60) | 78.10 (74.10 to 81.20) | | |
| Physical Functioning Cycle 7 Day 1 (n=122, 128) | 82.73 (79.76 to 85.71) | 80.78 (77.96 to 83.60) | | |
| Physical Functioning Cycle 8 Day 1 (n=119, 122) | 85.15 (82.75 to 87.56) | 81.75 (78.59 to 84.90) | | |
| Physical Functioning Cycle 9 Day 1 (n=121, 122) | 84.19 (81.57 to 86.81) | 83.99 (81.36 to 86.62) | | |
| Physical Functioning Cycle 10 Day 1 (n=114, 122) | 84.78 (82.16 to 87.40) | 83.88 (81.21 to 86.55) | | |
| Physical Functioning Cycle 11 Day 1 (n=119, 121) | 85.48 (83.18 to 87.77) | 84.24 (81.33 to 87.15) | | |
| Physical Functioning Cycle 12 Day 1 (n=119, 122) | 86.97 (84.66 to 89.29) | 83.44 (80.55 to 86.34) | | |

| | | | | |
|---|---|---|---|---|
| Physical Functioning Cycle 13 Day 1 (n=119, 121) | 86.16 (83.40 to 88.93) | 83.36 (80.27 to 86.45) | | |
| Physical Functioning Cycle 14 Day 1 (n=119, 117) | 86.22 (83.56 to 88.88) | 84.96 (82.18 to 87.73) | | |
| Physical Functioning Cycle 15 Day 1 (n=112, 116) | 84.69 (81.67 to 87.71) | 84.28 (81.23 to 87.34) | | |
| Physical Functioning Cycle 16 Day 1 (n=111, 114) | 87.19 (84.34 to 90.04) | 84.33 (81.37 to 87.29) | | |
| Physical Functioning SDC/ED (n=130, 137) | 84.21 (81.31 to 87.10) | 82.34 (79.24 to 85.43) | | |
| Physical Functioning SFU Month 3 (n=131, 142) | 85.29 (82.65 to 87.93) | 82.35 (79.29 to 85.41) | | |
| Physical Functioning SFU Month 6 (n=125,136) | 84.96 (82.15 to 87.77) | 84.17 (81.11 to 87.22) | | |
| Physical Functioning SFU Month 9 (n=116, 132) | 85.11 (82.46 to 87.77) | 83.48 (80.01 to 86.96) | | |
| Physical Functioning SFU Month 12 (n=111, 126) | 85.05 (81.79 to 88.30) | 83.17 (79.67 to 86.68) | | |
| Physical Functioning SFU Month 18 (n=102, 112) | 85.23 (81.63 to 88.82) | 84.29 (80.85 to 87.72) | | |
| Physical Functioning SFU Month 24 (n=82, 108) | 85.69 (82.05 to 89.33) | 85.43 (81.67 to 89.20) | | |
| Physical Functioning SFU Month 30 (n=65, 72) | 87.08 (83.41 to 90.75) | 84.54 (80.35 to 88.73) | | |
| Physical Functioning SFU Month 36 (n=62, 69) | 86.24 (81.63 to 90.84) | 85.80 (81.87 to 89.73) | | |
| Physical Functioning SFU Month 48 (n=2, 7) | 90.00 (-37.06 to 217.06) | 88.57 (75.88 to 101.26) | | |
| Role Functioning Baseline (n=166, 161) | 88.86 (85.67 to 92.04) | 89.44 (86.10 to 92.78) | | |
| Role Functioning Cycle 2 Day 1 (n=164, 157) | 80.39 (76.77 to 84.00) | 77.18 (73.47 to 80.88) | | |
| Role Functioning Cycle 3 Day 1 (n=152, 142) | 70.39 (65.96 to 74.83) | 69.48 (65.29 to 73.67) | | |
| Role Functioning Cycle 4 Day 1 (n=153, 149) | 61.11 (56.70 to 65.53) | 56.60 (51.56 to 61.64) | | |
| Role Functioning Cycle 5 Day 1 (n=146, 139) | 56.05 (51.06 to 61.04) | 51.08 (46.15 to 56.00) | | |
| Role Functioning Cycle 6 Day 1 (n=134, 132) | 66.17 (61.45 to 70.89) | 62.88 (57.70 to 68.06) | | |
| Role Functioning Cycle 7 Day 1 (n=122, 128) | 73.77 (69.21 to 78.33) | 69.92 (65.46 to 74.39) | | |
| Role Functioning Cycle 8 Day 1 (n=119, 122) | 77.59 (73.57 to 81.62) | 72.95 (68.13 to 77.77) | | |
| Role Functioning Cycle 9 Day 1 (n=121, 122) | 77.13 (72.98 to 81.29) | 74.32 (70.21 to 78.42) | | |
| Role Functioning Cycle 10 Day 1 (n=114, 122) | 78.51 (74.50 to 82.51) | 75.27 (70.94 to 79.61) | | |
| Role Functioning Cycle 11 Day 1 (n=119, 122) | 79.97 (76.41 to 83.53) | 75.68 (71.44 to 79.93) | | |
| Role Functioning Cycle 12 Day 1 (n=119, 122) | 81.79 (78.04 to 85.55) | 75.14 (70.52 to 79.75) | | |
| Role Functioning Cycle 13 Day 1 (n=119, 121) | 81.79 (78.16 to 85.42) | 74.38 (69.60 to 79.16) | | |
| Role Functioning Cycle 14 Day 1 (n=119, 117) | 80.81 (76.61 to 85.01) | 75.50 (70.60 to 80.40) | | |
| Role Functioning Cycle 15 Day 1 (n=112, 116) | 79.02 (75.14 to 82.90) | 77.59 (73.05 to 82.13) | | |
| Role Functioning Cycle 16 Day 1 (n=111, 114) | 83.03 (78.87 to 87.20) | 78.65 (74.05 to 83.26) | | |
| Role Functioning SDC/ED (n=130, 137) | 80.00 (76.07 to 83.93) | 74.09 (69.37 to 78.81) | | |

| | | | | |
|---|---|---|---|---|
| Role Functioning SFU Month 3 (n=131, 142) | 81.93 (78.24 to 85.63) | 75.47 (70.97 to 79.97) | | |
| Role Functioning SFU Month 6 (n=126, 136) | 78.53 (74.01 to 83.06) | 76.10 (71.38 to 80.83) | | |
| Role Functioning SFU Month 9 (n=116, 132) | 81.61 (77.90 to 85.32) | 76.39 (71.36 to 81.42) | | |
| Role Functioning SFU Month 12 (n=111, 126) | 81.68 (77.46 to 85.91) | 76.98 (71.47 to 82.50) | | |
| Role Functioning SFU Month 18 (n=102, 112) | 81.86 (76.88 to 86.85) | 77.98 (72.77 to 83.18) | | |
| Role Functioning SFU Month 24 (n=82, 108) | 79.47 (73.62 to 85.32) | 80.09 (75.03 to 85.15) | | |
| Role Functioning SFU Month 30 (n=65, 72) | 81.54 (75.51 to 87.56) | 78.24 (71.20 to 85.28) | | |
| Role Functioning SFU Month 36 (n=62, 69) | 85.48 (79.88 to 91.09) | 81.64 (75.23 to 88.05) | | |
| Role Functioning SFU Month 48 (n=2, 7) | 83.33 (-128.44 to 295.10) | 76.19 (-228.44 to 195.10) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Overall survival (OS) in Subpopulation with PD-L1-Positive Tumor Status

| | |
|---|---|
| End point title | Overall survival (OS) in Subpopulation with PD-L1-Positive Tumor Status |

End point description:

Overall survival (OS) defined as the time from randomization to the date of death from any cause in the subpopulation with PD-L1-positive tumor status. Note: 999999=not estimable.

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

End point timeframe:

From randomization and up to study final analysis data cut off on 28 September 2022.

| **End point values** | Placebo and Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 77 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 999999 (999999 to 999999) | 999999 (999999 to 999999) | | |

### Statistical analyses

| **Statistical analysis title** | OS Subpopulation with PD-L1-Positive Tumor Status |
|---|---|

Statistical analysis description:

Stratified analysis. Strata are: AJCC

stage at diagnosis (II vs. III).

| | |
|---|---|
| Comparison groups | Placebo and Chemotherapy v Atezolizumab and Chemotherapy |
| Number of subjects included in analysis | 152 |
| Analysis specification | Pre-specified |
| Analysis type | other[7] |
| Method | Stratified log-rank test |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.71 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.26 |
| upper limit | 1.91 |

Notes:

[7] - This study was not designed nor formally powered to demonstrate statistically significant improvements in the secondary efficacy endpoint of OS. The analyses of this secondary endpoint are descriptive in nature.

## Secondary: Overall survival (OS) in All Participants

| | |
|---|---|
| End point title | Overall survival (OS) in All Participants |

End point description:

Overall survival (OS) defined as the time from randomization to the date of death from any cause in all participants. Note: 999999=not estimable.

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

End point timeframe:

From randomization and up to study final analysis data cut off on 28 September 2022.

| End point values | Placebo and Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 168 | 165 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 999999 (999999 to 999999) | 999999 (999999 to 999999) | | |

## Statistical analyses

| Statistical analysis title | OS All Participants Statistical Analysis |
|---|---|

Statistical analysis description:

Stratified analysis. Strata are:
Tumor PD-L1 status (IC0 vs IC1/2/3) and AJCC stage at diagnosis (II vs. III).

| | |
|---|---|
| Comparison groups | Placebo and Chemotherapy v Atezolizumab and Chemotherapy |

| | |
|---|---|
| Number of subjects included in analysis | 333 |
| Analysis specification | Pre-specified |
| Analysis type | other[8] |
| Method | Stratified log-rank test |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.56 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.3 |
| upper limit | 1.04 |

Notes:

[8] - This study was not designed nor formally powered to demonstrate statistically significant improvements in the secondary efficacy endpoint of OS. The analyses of this secondary endpoint are descriptive in nature.

## Secondary: Mean Change From Baseline Scores for Function (Role, Physical) and GHS/HRQoL by Cycle and Between Treatment Arms as Assessed by the EORTC QLQ-C30

| | |
|---|---|
| End point title | Mean Change From Baseline Scores for Function (Role, Physical) and GHS/HRQoL by Cycle and Between Treatment Arms as Assessed by the EORTC QLQ-C30 |

End point description:

Mean change from baseline score in function (role, physical) and global health status(GHS)/ health-related quality of life (HRQoL) by cycle and between treatment arms as assessed by the functional and HRQoL scales of the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core30(QLQ C30). Analysis Population included all randomized participants with non-missing baseline assessment and at least one non-missing post-baseline assessment. Note: SDC=Study Drug Completion, ED=Early Discontinuation, SFU=Survival Follow-Up.

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

End point timeframe:

From randomization and up to study final analysis data cut off on 28 September 2022.

| **End point values** | Placebo and Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 167 | 161 | | |
| Units: Score on a 0-100 scale | | | | |
| arithmetic mean (confidence interval 95%) | | | | |
| GHS/QoL Cycle 2 Day 1 (n=164, 157) | -4.62 (-7.89 to -1.36) | -7.91 (-11.09 to -4.72) | | |
| GHS/QoL Cycle 3 Day 1 (n=152, 143) | -12.72 (-16.34 to -9.10) | -17.07 (-21.15 to -13.00) | | |
| GHS/QoL Cycle 4 Day 1 (n=153, 149) | -14.49 (-18.35 to -10.62) | -19.80 (-23.50 to -16.09) | | |
| GHS/QoL Cycle Cycle 5 Day 1 (n=147, 139) | -17.06 (-21.18 to -12.94) | -26.02 (-30.34 to -21.70) | | |
| GHS/QoL Cycle 6 Day 1 (n=134, 132) | -2.49 (-6.70 to 1.72) | -8.78 (-12.71 to -4.84) | | |
| GHS/QoL Cycle 7 Day 1 (n=122, 128) | -0.61 (-4.64 to 3.41) | -5.40 (-9.15 to -1.66) | | |
| GHS/QoL Cycle 8 Day 1 (n=119, 122) | 0.77 (-3.30 to 4.84) | -6.69 (-10.49 to -2.90) | | |

| | | | | |
|---|---|---|---|---|
| GHS/QoL Cycle 9 Day 1 (n=121,121) | -0.28 (-4.10 to 3.55) | -6.13 (-9.94 to -2.32) | | |
| GHS/QoL Cycle 10 Day 1 (n=114,122) | -1.17 (-5.02 to 2.68) | -8.40 (-12.50 to -4.30) | | |
| GHS/QoL Cycle 11 Day 1 (n=119,122) | 0.35 (-3.42 to 4.13) | -7.04 (-11.11 to -2.96) | | |
| GHS/QoL Cycle 12 Day 1 (n=119,122 ) | -0.63 (-4.64 to 3.38) | -6.56 (-10.48 to -2.64) | | |
| GHS/QoL Cycle 13 Day 1 (n=119,121) | -1.26 (-5.19 to 2.67) | -5.85 (-9.83 to -1.88) | | |
| GHS/QoL Cycle 14 Day 1 (n=119,116) | -1.05 (-4.95 to 2.85) | -7.47 (-11.44 to -3.50) | | |
| GHS/QoL Cycle 15 Day 1 (n=112,116) | 0.00 (-4.21 to 4.21) | -4.67 (-8.71 to -0.63) | | |
| GHS/QoL Cycle 16 Day 1 (n=111,114) | 2.10 (-1.66 to 5.86) | -3.73 (-7.93 to 0.48) | | |
| GHS/QoL SDC/ED (n=130,137) | 0.06 (-3.99 to 4.12) | -6.20 (-10.47 to -1.94) | | |
| GHS/QoL SFU Month 3 (n=131,142) | 0.64 (-3.54 to 4.81) | -6.57 (-10.28 to -2.87) | | |
| GHS/QoL SFU Month 6 (n=125,136) | -2.00 (-6.16 to 2.16) | -3.37 (-7.24 to 0.50) | | |
| GHS/QoL SFU Month 9 (n=116,132) | 0.93 (-5.26 to 3.39) | -4.42 (-8.07 to -0.77) | | |
| GHS/QoL SFU Month 12 (n=111,126) | -1.65 (-5.91 to 2.61) | -4.50 (-8.67 to -0.32) | | |
| GHS/QoL SFU Month 18 (n=102,112) | -0.98 (-6.10 to 4.14) | -4.17 (-8.67 to 0.34) | | |
| GHS/QoL SFU Month 24 (n=83, 108) | 1.31 (-3.50 to 6.12) | -6.17 (-10.96 to -1.39) | | |
| GHS/QoL SFU Month 30 (n=65, 72) | -2.18 (-8.05 to 3.69) | -9.14 (-14.26 to -4.03) | | |
| GHS/QoL SFU Month 36 (n=62,69) | -1.08 (-6.42 to 4.27) | -5.56 (-11.22 to 0.11) | | |
| GHS/QoL SFU Month 48 (n=2,7) | -25.00 (-342.66 to 292.66) | -21.43 (-37.99 to -4.86) | | |
| Physical Functioning Cycle 2 Day 1 (n=163, 157) | -6.37 (-8.58 to -4.16) | -5.73 (-8.18 to -3.29) | | |
| Physical Functioning Cycle 3 Day 1 (n=151, 142) | -12.17 (-15.43 to -8.92) | -12.90 (-16.62 to -9.17) | | |
| Physical Functioning Cycle 4 Day 1 (n=151, 149) | -19.48 (-22.51 to -16.45) | -21.68 (-25.66 to -17.70) | | |
| Physical Functioning Cycle 5 Day 1 (n=145, 139) | -21.59 (-25.17 to -18.01) | -26.43 (-30.61 to -22.25) | | |
| Physical Functioning Cycle 6 Day 1 (n=134, 132) | -10.20 (-13.46 to -6.94) | -12.20 (-15.39 to -9.00) | | |
| Physical Functioning Cycle 7 Day 1 (n=122,128) | -7.43 (-10.48 to -4.38) | -8.96 (-12.22 to -5.69) | | |
| Physical Functioning Cycle 8 Day 1 (n=119,122) | -4.80 (-7.52 to -2.09) | -7.70 (-11.21 to -4.19) | | |
| Physical Functioning Cycle 9 Day 1 (n=121,122) | -5.40 (-8.20 to -2.60) | -5.74 (-9.04 to -2.44) | | |
| Physical Functioning Cycle 10 Day 1 (n=114,122) | -4.87 (-7.82 to -1.92) | -6.17 (-9.25 to -3.10) | | |
| Physical Functioning Cycle 11 Day 1 (n=119,121) | -3.99 (-6.77 to -1.21) | -5.73 (-9.09 to -2.37) | | |
| Physical Functioning Cycle 12 Day 1 (n=119,122) | -2.59 (-5.39 to 0.21) | -6.61 (-9.60 to -3.62) | | |
| Physical Functioning Cycle 13 Day 1 (n=119,121) | -3.63 (-6.77 to -0.48) | -6.72 (-10.01 to -3.43) | | |

| | | | | |
|---|---|---|---|---|
| Physical Functioning Cycle 14 Day 1 (n=119,117) | -3.42 (-6.33 to -0.51) | -5.07 (-8.25 to -1.89) | | |
| Physical Functioning Cycle 15 Day 1 (n=112,116) | -4.24 (-7.59 to -0.89) | -5.89 (-9.22 to -2.56) | | |
| Physical Functioning Cycle 16 Day 1 (n=111,114) | -2.42 (-5.70 to 0.86) | -5.79 (-9.05 to -2.53) | | |
| Physical Functioning SDC/ED (n=130,137) | -5.58 (-8.88 to -2.27) | -8.66 (-12.12 to -5.21) | | |
| Physical Functioning SFU Month 3 (n=131,142) | -4.16 (-6.77 to -1.55) | -8.54 (-11.83 to -5.26) | | |
| Physical Functioning SFU Month 6 (n=125,136) | -5.21 (-7.90 to -2.53) | -6.91 (-10.10 to -3.72) | | |
| Physical Functioning SFU Month 9 (n=116,132) | -3.97 (-6.65 to -1.28) | -7.78 (-11.20 to -4.36) | | |
| Physical Functioning SFU Month 12 (n=111,126) | -4.43 (-7.23 to -1.62) | -7.46 (-11.07 to -3.85) | | |
| Physical Functioning SFU Month 18 (n=102,112) | -4.90 (-8.58 to -1.22) | -6.61 (-10.17 to -3.05) | | |
| Physical Functioning SFU Month 24 (n=82,108) | -4.07 (-7.64 to -0.49) | -6.30 (-9.94 to -2.65) | | |
| Physical Functioning SFU Month 30 (n=65,72) | -3.36 (-6.90 to 0.18) | -10.46 (-14.68 to -6.25) | | |
| Physical Functioning SFU Month 36 (n=62,69) | -4.06 (-8.93 to 0.81) | -8.70 (-12.47 to -4.92) | | |
| Physical Functioning SFU Month 48 (n=2,7) | -3.33 (-45.69 to 39.02) | -11.43 (-24.12 to 1.26) | | |
| Role Functioning Cycle 2 Day 1 (n=163, 157) | -8.08 (-12.05 to -4.11) | -12.42 (-16.70 to -8.14) | | |
| Role Functioning Cycle 3 Day 1 (n=151, 142) | -19.54 (-24.57 to -14.50) | -19.84 (-24.92 to -14.76) | | |
| Role Functioning Cycle 4 Day 1 (n=152, 149) | -28.29 (-33.49 to -23.09) | -33.56 (-39.19 to -27.93) | | |
| Role Functioning Cycle 5 Day 1 (n=145, 139) | -32.99 (-38.45 to -27.53) | -38.97 (-44.44 to -33.50) | | |
| Role Functioning Cycle 6 Day 1 (n=134, 132) | -22.39 (-27.55 to -17.23) | -26.14 (-31.45 to -20.83) | | |
| Role Functioning Cycle 7 Day 1 (n=122,128) | -14.21 (-19.06 to -9.35) | -18.36 (-23.36 to -13.36) | | |
| Role Functioning Cycle 8 Day 1 (n=119,122) | -10.50 (-15.16 to -5.85) | -14.89 (-20.37 to -9.41) | | |
| Role Functioning Cycle 9 Day 1 (n=121,122) | -10.74 (-15.21 to -6.28) | -13.80 (-19.13 to -8.47) | | |
| Role Functioning Cycle 10 Day 1 (n=114,122) | -9.36 (-13.94 to -4.77) | -13.39 (-18.13 to -8.64) | | |
| Role Functioning Cycle 11 Day 1 (n=119,122) | -8.26 (-12.65 to -3.88) | -12.98 (-17.53 to -8.43) | | |
| Role Functioning Cycle 12 Day 1 (n=119,122) | -6.86 (-11.40 to -2.33) | -13.52 (-18.06 to -8.99) | | |
| Role Functioning Cycle 13 Day 1 (n=119,121) | -6.30 (-10.16 to -2.44) | -14.46 (-19.69 to -9.24) | | |
| Role Functioning Cycle 14 Day 1 (n=119,117) | -7.28 (-11.77 to -2.80) | -13.82 (-18.80 to -8.84) | | |
| Role Functioning Cycle 15 Day 1 (n=112,116) | -8.63 (-13.14 to -4.12) | -11.78 (-16.96 to -6.60) | | |
| Role Functioning Cycle 16 Day 1 (n=111,114) | -4.65 (-9.70 to 0.39) | -10.82 (-15.56 to -6.07) | | |
| Role Functioning SDC/ED (n=130,137) | -8.46 (-13.54 to -3.38) | -16.42 (-21.64 to -11.21) | | |
| Role Functioning SFU Month 3 (n=131,142) | -5.98 (-10.57 to -1.39) | -14.44 (-19.35 to -9.53) | | |
| Role Functioning SFU Month 6 (n=125,136) | -10.67 (-15.66 to -5.68) | -13.97 (-18.84 to -9.10) | | |

| | | | | |
|---|---|---|---|---|
| Role Functioning SFU Month 9 (n=116,132) | -7.61 (-12.23 to -3.00) | -13.76 (-18.45 to -9.08) | | |
| Role Functioning SFU Month 12 (n=111,126) | -7.66 (-11.90 to -3.41) | -12.83 (-18.13 to -7.53) | | |
| Role Functioning SFU Month 18 (n=102,112) | -7.03 (-12.54 to -1.51) | -12.05 (-17.15 to -6.95) | | |
| Role Functioning SFU Month 24 (n=82,108) | -9.96 (-15.85 to -4.07) | -10.96 (-16.19 to -5.72) | | |
| Role Functioning SFU Month 30 (n=52,72) | -8.72 (-15.45 to -1.98) | -16.44 (-23.12 to -9.75) | | |
| Role Functioning SFU Month 36 (n=62,69) | -5.65 (-12.45 to 1.16) | -12.56 (-18.94 to -6.18) | | |
| Role Functioning SFU Month 48 (n=2,7) | -16.67 (-228.44 to 195.10) | -21.43 (-47.70 to 4.84) | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Minimum Observed Serum Atezolizumab Concentration (Cmin)**

| End point title | Minimum Observed Serum Atezolizumab Concentration |
|---|---|

End point description:

Minimum observed serum atezolizumab concentration.

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

End point timeframe:

Pre-dose on Day 1 of Cycles 2, 3, 4, 6, 8, 12, and 16 (cycle length = 28 days from Cycles 1 to 5, and 21 days from Cycles 6 to 16)

Notes:

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

| **End point values** | Atezolizumab and Chemotherapy | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 164 | | | |
| Units: µg/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Cycle 2 Day 1 | 142 (± 54.3) | | | |
| Cycle 3 Day 1 | 189 (± 64.2) | | | |
| Cycle 4 Day 1 | 207 (± 77.3) | | | |
| Cycle 6 Day 1 | 78.7 (± 50.3) | | | |
| Cycle 8 Day 1 | 204 (± 62.7) | | | |
| Cycle 12 Day 1 | 267 (± 81.1) | | | |
| Cycle 16 Day 1 | 303 (± 89.1) | | | |

**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[10] |
|---|---|

End point description:

Percentage of participants with anti-drug antibodies (ADAs) to atezolizumab.

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

End point timeframe:

Baseline up to approximately 20 months

Notes:

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

| End point values | Atezolizumab and Chemotherapy | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 162 | | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Baseline evaluable participants | 2.5 | | | |
| Post-baseline evaluable participants | 13.4 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum Observed Serum Atezolizumab Concentration (Cmax)

| End point title | Maximum Observed Serum Atezolizumab Concentration |
|---|---|

End point description:

Maximum observed atezolizumab concentration (Cmax).

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

End point timeframe:

Day 1 of Cycle 1 post dose (cycle length = 28 days)

Notes:

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

| End point values | Atezolizumab and Chemotherapy | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 164 | | | |
| Units: µg/mL | | | | |
| arithmetic mean (standard deviation) | 334 (± 63.3) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With at Least One Adverse Events (AEs)

| End point title | Percentage of Participants With at Least One Adverse Events (AEs) |
|---|---|

End point description:

Percentage of participants with at least one adverse event.

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

End point timeframe:

Baseline up to approximately 62 months

| End point values | Placebo and Chemotherapy | Atezolizumab and Chemotherapy | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 167 | 164 | | |
| Units: Percentage of participants | 100 | 100 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the first study drug and up to study final analysis data cut off on 28 September 2022.

Adverse event reporting additional description:

Safety evaluable population is defined as all participants who received at least one dose of study medication.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 25.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Atezolizumab + Nab-paclitaxel + AC |

Reporting group description:

Participants received atezolizumab (840 milligrams [mg]) via intravenous (IV) infusion every 2 weeks in combination with nab-paclitaxel (125 milligrams per square meter [mg/m^2]) via IV infusion every week for 12 weeks, followed by atezolizumab (840 mg) every 2 weeks in combination with doxorubicin (60 mg/m^2) and cyclophosphamide (600 mg/m^2) every 2 weeks via IV infusions with filgrastim/pegfilgrastim support for 4 doses. Participants continued to receive unblinded atezolizumab post-surgery at a fixed dose of 1200 mg by IV infusion every 3 weeks for 11 doses, for a total of approximately 12 months of atezolizumab therapy.

| | |
|---|---|
| Reporting group title | Placebo + Nab-paclitaxel + AC |

Reporting group description:

Participants received placebo matched to atezolizumab via IV infusion every 2 weeks in combination with nab-paclitaxel (125 mg/m^2) via IV infusion every week for 12 weeks, followed by placebo matched to atezolizumab every 2 weeks in combination with doxorubicin (60 mg/m^2) and cyclophosphamide (600 mg/m^2) every 2 weeks via IV infusions with filgrastim/pegfilgrastim support for 4 doses. Participants will continue to be followed after surgery.

| **Serious adverse events** | Atezolizumab + Nab-paclitaxel + AC | Placebo + Nab-paclitaxel + AC | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 59 / 164 (35.98%) | 36 / 167 (21.56%) | |
| number of deaths (all causes) | 16 | 28 | |
| number of deaths resulting from adverse events | 0 | 1 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Tumour haemorrhage | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Embolism | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombosis | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 164 (2.44%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Respiratory, thoracic and mediastinal disorders | | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fracture | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis chemical | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Post procedural haematoma | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Road traffic accident | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Wound dehiscence | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Syncope | | | |
| subjects affected / exposed | 3 / 164 (1.83%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polyneuropathy | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral motor neuropathy | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Guillain-Barre syndrome | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 164 (0.61%) | 3 / 167 (1.80%) | |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 16 / 164 (9.76%) | 13 / 167 (7.78%) | |
| occurrences causally related to treatment / all | 16 / 18 | 14 / 14 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Obstructive pancreatitis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 164 (1.22%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 2 / 164 (1.22%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal distension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (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 function abnormal | | | |
| subjects affected / exposed | 3 / 164 (1.83%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatomyositis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| Renal infarct | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Hypopituitarism | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Candida infection | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacillus bacteraemia | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal infection | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Encephalitis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mastitis | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periorbital cellulitis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (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 | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 6 / 164 (3.66%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 4 / 6 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pyelonephritis acute | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (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 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular device infection | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Vitamin D deficiency | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 164 (0.00%) | 1 / 167 (0.60%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 0 / 167 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 164 (0.61%) | 2 / 167 (1.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Atezolizumab + Nab-paclitaxel + AC | Placebo + Nab-paclitaxel + AC | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 162 / 164 (98.78%) | 167 / 167 (100.00%) | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 15 / 164 (9.15%) | 17 / 167 (10.18%) | |
| occurrences (all) | 27 | 29 | |
| Hot flush | | | |
| subjects affected / exposed | 28 / 164 (17.07%) | 17 / 167 (10.18%) | |
| occurrences (all) | 32 | 20 | |
| General disorders and administration site conditions | | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 18 / 164 (10.98%) | 15 / 167 (8.98%) | |
| occurrences (all) | 24 | 19 | |
| Asthenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 42 / 164 (25.61%) | 36 / 167 (21.56%) | |
| occurrences (all) | 66 | 40 | |
| Fatigue | | | |
| subjects affected / exposed | 65 / 164 (39.63%) | 65 / 167 (38.92%) | |
| occurrences (all) | 94 | 86 | |
| Malaise | | | |
| subjects affected / exposed | 15 / 164 (9.15%) | 17 / 167 (10.18%) | |
| occurrences (all) | 35 | 18 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 24 / 164 (14.63%) | 24 / 167 (14.37%) | |
| occurrences (all) | 30 | 27 | |
| Pain | | | |
| subjects affected / exposed | 20 / 164 (12.20%) | 11 / 167 (6.59%) | |
| occurrences (all) | 22 | 11 | |
| Pyrexia | | | |
| subjects affected / exposed | 37 / 164 (22.56%) | 21 / 167 (12.57%) | |
| occurrences (all) | 55 | 25 | |
| Reproductive system and breast disorders | | | |
| Breast pain | | | |
| subjects affected / exposed | 17 / 164 (10.37%) | 15 / 167 (8.98%) | |
| occurrences (all) | 19 | 15 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 41 / 164 (25.00%) | 32 / 167 (19.16%) | |
| occurrences (all) | 52 | 39 | |
| Dyspnoea | | | |
| subjects affected / exposed | 23 / 164 (14.02%) | 20 / 167 (11.98%) | |
| occurrences (all) | 25 | 22 | |
| Epistaxis | | | |
| subjects affected / exposed | 25 / 164 (15.24%) | 24 / 167 (14.37%) | |
| occurrences (all) | 26 | 26 | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 19 / 164 (11.59%) | 18 / 167 (10.78%) | |
| occurrences (all) | 20 | 19 | |
| Rhinorrhoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 10 / 164 (6.10%) | 0 / 167 (0.00%) | |
| occurrences (all) | 12 | 0 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 12 / 164 (7.32%) | 11 / 167 (6.59%) | |
| occurrences (all) | 13 | 11 | |
| Depression | | | |
| subjects affected / exposed | 11 / 164 (6.71%) | 6 / 167 (3.59%) | |
| occurrences (all) | 11 | 6 | |
| Insomnia | | | |
| subjects affected / exposed | 49 / 164 (29.88%) | 29 / 167 (17.37%) | |
| occurrences (all) | 61 | 30 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 39 / 164 (23.78%) | 35 / 167 (20.96%) | |
| occurrences (all) | 63 | 53 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 37 / 164 (22.56%) | 28 / 167 (16.77%) | |
| occurrences (all) | 64 | 44 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 14 / 164 (8.54%) | 4 / 167 (2.40%) | |
| occurrences (all) | 19 | 4 | |
| Blood lactate dehydrogenase increased | | | |
| subjects affected / exposed | 10 / 164 (6.10%) | 7 / 167 (4.19%) | |
| occurrences (all) | 11 | 7 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 29 / 164 (17.68%) | 30 / 167 (17.96%) | |
| occurrences (all) | 60 | 67 | |
| Weight decreased | | | |
| subjects affected / exposed | 15 / 164 (9.15%) | 8 / 167 (4.79%) | |
| occurrences (all) | 17 | 8 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 14 / 164 (8.54%) | 15 / 167 (8.98%) | |
| occurrences (all) | 33 | 35 | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|---|---|---|
| Infusion related reaction | | | |
| subjects affected / exposed | 16 / 164 (9.76%) | 10 / 167 (5.99%) | |
| occurrences (all) | 28 | 16 | |
| Procedural pain | | | |
| subjects affected / exposed | 14 / 164 (8.54%) | 2 / 167 (1.20%) | |
| occurrences (all) | 17 | 2 | |
| Radiation skin injury | | | |
| subjects affected / exposed | 32 / 164 (19.51%) | 0 / 167 (0.00%) | |
| occurrences (all) | 32 | 0 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 20 / 164 (12.20%) | 15 / 167 (8.98%) | |
| occurrences (all) | 33 | 16 | |
| Dysgeusia | | | |
| subjects affected / exposed | 16 / 164 (9.76%) | 25 / 167 (14.97%) | |
| occurrences (all) | 20 | 27 | |
| Headache | | | |
| subjects affected / exposed | 51 / 164 (31.10%) | 36 / 167 (21.56%) | |
| occurrences (all) | 86 | 46 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 40 / 164 (24.39%) | 34 / 167 (20.36%) | |
| occurrences (all) | 48 | 42 | |
| Paraesthesia | | | |
| subjects affected / exposed | 12 / 164 (7.32%) | 19 / 167 (11.38%) | |
| occurrences (all) | 13 | 22 | |
| Polyneuropathy | | | |
| subjects affected / exposed | 10 / 164 (6.10%) | 14 / 167 (8.38%) | |
| occurrences (all) | 10 | 15 | |
| Taste disorder | | | |
| subjects affected / exposed | 10 / 164 (6.10%) | 13 / 167 (7.78%) | |
| occurrences (all) | 11 | 13 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 58 / 164 (35.37%) | 42 / 167 (25.15%) | |
| occurrences (all) | 65 | 45 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| Leukopenia | | | |
| subjects affected / exposed | 23 / 164 (14.02%) | 17 / 167 (10.18%) | |
| occurrences (all) | 46 | 29 | |
| Anaemia | | | |
| subjects affected / exposed | 64 / 164 (39.02%) | 65 / 167 (38.92%) | |
| occurrences (all) | 89 | 80 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 13 / 164 (7.93%) | 5 / 167 (2.99%) | |
| occurrences (all) | 16 | 6 | |
| Neutropenia | | | |
| subjects affected / exposed | 65 / 164 (39.63%) | 59 / 167 (35.33%) | |
| occurrences (all) | 141 | 123 | |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 13 / 164 (7.93%) | 6 / 167 (3.59%) | |
| occurrences (all) | 13 | 6 | |
| Lacrimation increased | | | |
| subjects affected / exposed | 18 / 164 (10.98%) | 18 / 167 (10.78%) | |
| occurrences (all) | 21 | 18 | |
| Vision blurred | | | |
| subjects affected / exposed | 16 / 164 (9.76%) | 11 / 167 (6.59%) | |
| occurrences (all) | 16 | 12 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 23 / 164 (14.02%) | 16 / 167 (9.58%) | |
| occurrences (all) | 29 | 21 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 21 / 164 (12.80%) | 13 / 167 (7.78%) | |
| occurrences (all) | 23 | 16 | |
| Diarrhoea | | | |
| subjects affected / exposed | 74 / 164 (45.12%) | 74 / 167 (44.31%) | |
| occurrences (all) | 110 | 117 | |
| Dry mouth | | | |
| subjects affected / exposed | 10 / 164 (6.10%) | 5 / 167 (2.99%) | |
| occurrences (all) | 11 | 6 | |
| Dyspepsia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 19 / 164 (11.59%) | 21 / 167 (12.57%) | |
| occurrences (all) | 22 | 23 | |
| Nausea | | | |
| subjects affected / exposed | 108 / 164 (65.85%) | 110 / 167 (65.87%) | |
| occurrences (all) | 218 | 189 | |
| Stomatitis | | | |
| subjects affected / exposed | 40 / 164 (24.39%) | 29 / 167 (17.37%) | |
| occurrences (all) | 48 | 32 | |
| Vomiting | | | |
| subjects affected / exposed | 63 / 164 (38.41%) | 51 / 167 (30.54%) | |
| occurrences (all) | 105 | 70 | |
| Constipation | | | |
| subjects affected / exposed | 51 / 164 (31.10%) | 55 / 167 (32.93%) | |
| occurrences (all) | 74 | 64 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 125 / 164 (76.22%) | 129 / 167 (77.25%) | |
| occurrences (all) | 127 | 132 | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 6 / 164 (3.66%) | 10 / 167 (5.99%) | |
| occurrences (all) | 8 | 10 | |
| Dry skin | | | |
| subjects affected / exposed | 18 / 164 (10.98%) | 13 / 167 (7.78%) | |
| occurrences (all) | 20 | 13 | |
| Erythema | | | |
| subjects affected / exposed | 15 / 164 (9.15%) | 5 / 167 (2.99%) | |
| occurrences (all) | 17 | 5 | |
| Nail discolouration | | | |
| subjects affected / exposed | 26 / 164 (15.85%) | 29 / 167 (17.37%) | |
| occurrences (all) | 28 | 29 | |
| Nail disorder | | | |
| subjects affected / exposed | 21 / 164 (12.80%) | 10 / 167 (5.99%) | |
| occurrences (all) | 22 | 10 | |
| Pruritus | | | |
| subjects affected / exposed | 36 / 164 (21.95%) | 25 / 167 (14.97%) | |
| occurrences (all) | 49 | 31 | |

| | | | |
|---|---|---|---|
| Rash | | | |
| subjects affected / exposed | 52 / 164 (31.71%) | 42 / 167 (25.15%) | |
| occurrences (all) | 68 | 53 | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 12 / 164 (7.32%) | 12 / 167 (7.19%) | |
| occurrences (all) | 12 | 14 | |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 22 / 164 (13.41%) | 0 / 167 (0.00%) | |
| occurrences (all) | 22 | 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 50 / 164 (30.49%) | 42 / 167 (25.15%) | |
| occurrences (all) | 76 | 61 | |
| Back pain | | | |
| subjects affected / exposed | 24 / 164 (14.63%) | 20 / 167 (11.98%) | |
| occurrences (all) | 27 | 24 | |
| Bone pain | | | |
| subjects affected / exposed | 13 / 164 (7.93%) | 11 / 167 (6.59%) | |
| occurrences (all) | 14 | 12 | |
| Myalgia | | | |
| subjects affected / exposed | 51 / 164 (31.10%) | 40 / 167 (23.95%) | |
| occurrences (all) | 86 | 49 | |
| Pain in extremity | | | |
| subjects affected / exposed | 27 / 164 (16.46%) | 19 / 167 (11.38%) | |
| occurrences (all) | 36 | 26 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 23 / 164 (14.02%) | 14 / 167 (8.38%) | |
| occurrences (all) | 29 | 17 | |
| Paronychia | | | |
| subjects affected / exposed | 19 / 164 (11.59%) | 21 / 167 (12.57%) | |
| occurrences (all) | 20 | 21 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 23 / 164 (14.02%) | 16 / 167 (9.58%) | |
| occurrences (all) | 30 | 16 | |

| | | | |
|---|---|---|---|
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 18 / 164 (10.98%)<br>25 | 11 / 167 (6.59%)<br>11 | |
| Metabolism and nutrition disorders<br>Decreased appetite<br>subjects affected / exposed<br>occurrences (all) | 28 / 164 (17.07%)<br>37 | 33 / 167 (19.76%)<br>36 | |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all) | 12 / 164 (7.32%)<br>24 | 7 / 167 (4.19%)<br>9 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 04 May 2017 | Protocol was amended to add a cardiac safety cohort. A mandatory baseline pulmonary function evaluation conducted via spirometry has been added to the Schedule of Activities. It has been clarified that patients who do not initially meet all eligibility criteria, other than TNBC status, may be rescreened only once. Pregnancy reporting timeline requirement for nab-paclitaxel has been amended to be 1 month after last dose. Event-free survival (EFS) has been clarified, EFS is defined as "the time from randomization to the first documented occurrence of disease recurrence, disease progression, or death from any cause." Language has been updated to indicate that if nab-paclitaxel is discontinued due to any reason, patients can proceed to AC chemotherapy plus atezolizumab/placebo at the discretion of the investigator. If AC chemotherapy is discontinued, the date of surgery can be brought forward and patients can proceed to surgery at the discretion of the investigator. |
| 11 May 2018 | Protocol was amended to include addition of history of cerebrovascular accident within 12 months prior to randomization as an exclusion criteria. Ductal carcinoma in situ (DCIS) is no longer an exception to the exclusion criterion of history of other malignancy within 5 years prior to screening as there was already a dedicated section to DCIS. History of a cerebrovascular accident within 12 months prior to randomization has been added as an exclusion criterion. It has been clarified that anticipation of need for a major surgical procedure as an exclusion criterion does not pertain to anticipated breast surgery. The risks associated with atezolizumab have been updated to include hypophysitis and myocarditis as adverse events. The safety profile of and risk management guidelines for nab-paclitaxel has been updated or clarified to include febrile neutropenia, infections, and depression. |
| 10 October 2018 | Protocol was amended to add an adaptive two stage design using accumulating data to inform the study. Study duration and recruitment period were updated to reflect potential change in study duration. The primary efficacy objective was modified to include the endpoint of pCR in the subpopulation with the PD-L1-positive tumor status (moved from the secondary efficacy objective). The secondary efficacy endpoints were modified to include disease-free survival. Lists of risks for atezolizumab and guidelines for managing participants who experience atezolizumab-associated adverse events have been revised to include nephritis. |
| 07 June 2019 | Protocol was amended to clarify the baseline staging and surgical management of clinically enlarged and/or suspicious internal mammary and infraclavicular and/or supraclavicular lymph nodes. Language has been modified to reflect the fact that systemic immune activation is a potential risk with atezolizumab, regardless of whether atezolizumab is given alone or in combination with other immunomodulating agents. The lists of risks associated with doxorubicin and cyclophosphamide have been updated to align with the latest safety information available on their corresponding SmPCs. |

| | |
|---|---|
| 11 February 2020 | Protocol was amended to include changing "immune-related" to "immune-mediated" when describing events associated with atezolizumab. Systemic immune activation has been replaced by hemophagocytic lymphohistiocytosis and macrophage activation syndrome in the list of potential risks for atezolizumab and the management guidelines for systemic immune activation have been replaced with management guidelines for hemophagocytic lymphohistiocytosis and macrophage activation syndrome. In addition, systemic immune activation has been removed from the list of adverse events of special interest. To align with the nab-paclitaxel (Abraxane®) prescribing information, the risk of tumor lysis syndrome has been included. The atezolizumab adverse event management guidelines have been revised to add laboratory and cardiac imaging abnormalities as signs or symptoms that are suggestive of myocarditis. The management guidelines for infusion-related reactions associated with atezolizumab have been updated to include guidelines for cytokine-release syndrome (CRS). |
| 08 February 2021 | Protocol was amended to include revision to the list of identified risks for atezolizumab to include severe cutaneous adverse reactions. Revision to Appendix 8 included caution should be used when considering atezolizumab in participants who have previously experienced a severe or life-threatening skin adverse reaction while receiving another immunostimulatory anti-cancer agent. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study was not designed nor formally powered to demonstrate statistically significant improvements in the secondary efficacy endpoints of EFS, DFS and OS. The analyses of these secondary endpoints are descriptive in nature.

Notes: