# Clinical trial results:
# A phase III, randomized, double-blind, placebo-controlled clinical trial to evaluate the efficacy and safety of atezolizumab or placebo in combination with neoadjuvant doxorubicin + cyclophosphamide followed by paclitaxel + trastuzumab + pertuzumab in early HER2-positive breast cancer.

## Summary

| | |
|---|---|
| EudraCT number | 2018-001881-40 |
| Trial protocol | DE CZ ES PL IT |
| Global end of trial date | |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 13 March 2022 |
| First version publication date | 06 February 2022 |
| Version creation reason | |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | BO40747 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03726879 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

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

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Interim |
| Date of interim/final analysis | 05 February 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 05 February 2021 |
| Global end of trial reached? | No |

Notes:

## General information about the trial

Main objective of the trial:

This study (also known as IMpassion050) is evaluating the efficacy and safety of atezolizumab compared with placebo when given in combination with neoadjuvant dose-dense anthracycline (doxorubicin) + cyclophosphamide followed by paclitaxel + trastuzumab + pertuzumab (ddAC-PacHP) in patients with early HER2-positive breast cancer (T2-4, N1-3, M0).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 11 January 2019 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy |
| Long term follow-up duration | 36 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Brazil: 75 |
| Country: Number of subjects enrolled | Canada: 26 |
| Country: Number of subjects enrolled | Germany: 33 |
| Country: Number of subjects enrolled | Italy: 46 |
| Country: Number of subjects enrolled | Japan: 39 |
| Country: Number of subjects enrolled | Korea, Republic of: 33 |
| Country: Number of subjects enrolled | Poland: 31 |
| Country: Number of subjects enrolled | Russian Federation: 45 |
| Country: Number of subjects enrolled | Spain: 59 |
| Country: Number of subjects enrolled | Taiwan: 49 |
| Country: Number of subjects enrolled | United States: 8 |
| Country: Number of subjects enrolled | Czechia: 10 |
| Worldwide total number of subjects | 454 |
| EEA total number of subjects | 179 |

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) | 411 |
| From 65 to 84 years | 43 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 74 centers in 12 countries.

### Pre-assignment

Screening details:

A total of 669 participants were screened, of which a total of 454 participants were enrolled.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Atezolizumab +ddAC-PacHP |

Arm description:

Participants received atezolizumab (atezo) 840 mg IV Q2W for 4 cycles during neoadjuvant phase with ddAC (doxorubicin 60 mg/m2 & cyclophosphamide 600 mg/m2 IV), followed by atezo 1200 mg IV Q3W for 4 cycles with paclitaxel 80 mg/m2 IV weekly for 12 continuous weeks, trastuzumab 6 mg/kg IV (with initial 8mg/kg IV loading dose) Q3W for 4 cycles, & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W for 4 cycles. During adjuvant phase, participants continued to receive following study treatments Q3W to complete up to 1 year HER2-target therapy inclusive of therapy given both in neoadjuvant and adjuvant setting: atezo 1200 mg IV Q3W, trastuzumab 6 mg/kg IV (with initial 8-mg/kg IV loading dose) Q3W, & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W. Participants who did not achieve pCR had option of receiving blinded atezo+trastuzumab emtansine post surgery for 14 cycles. In response to USM DIL dated 3 Feb 2021 treatment with atezo was discontinued.

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

Dosage and administration details:

Atezolizumab was administered by intravenous infusion at a dose of 840 milligrams (mg) every 2 weeks (Q2W) for 4 cycles during neoadjuvant phase followed by atezolizumab 1200 mg IV every 3 weeks (Q3W) for 4 cycles. During the adjuvant phase, participants continued to receive atezolizumab 1200 mg IV Q3W. In response to USM DIL dated 3 Feb 2021 treatment with atezolizumab must be discontinued.

| | |
|---|---|
| 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 by IV infusion in the neoadjuvant setting at a dosage of 60 mg/m^2 on Day 2 of a 14 day cycle for cylces 1-4.

| | |
|---|---|
| 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 by IV infusion in the neoadjuvant setting at a dosage of 600 mg/m^2 on Day 2 of a 14 day cycle for cylces 1-4.

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

Dosage and administration details:

Paclitaxel was administered by IV infusion in the neoadjuvant setting at a dosage of 80 mg/m^2 for 12 continuous weeks (cycles 5-8).

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

Dosage and administration details:

Trastuzumab was administered on Day 1 of a 21-day cycle as an 8-mg/kilogram(kg) loading dose and then a 6 mg/kg IV Q3W up to 52 weeks.

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

Dosage and administration details:

Pertuzumab was administered on Day 1 of a 21-day cycle as a fixed non-weight-based dose of 840-mg IV loading dose and then 420 mg IV Q3W up to 52 weeks.

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

Dosage and administration details:

Trastuzumab emtansine was administered at a dose of 3.6 mg/kg IV infusion Q3W.

| | |
|---|---|
| **Arm title** | Placebo + ddAC-PacHP |

Arm description:

Participants received placebo 840 mg IV Q2W for 4 cycles during neoadjuvant phase with ddAC (doxorubicin 60 mg/m2 & cyclophosphamide 600 mg/m2 IV), followed by placebo 1200 mg IV Q3W for 4 cycles with paclitaxel 80 mg/m2 IV weekly for 12 continuous weeks, trastuzumab 6 mg/kg IV (with initial 8-mg/kg IV loading dose) Q3W for 4 cycles & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W for 4 cycles. During adjuvant phase, participants continued to receive following study treatments Q3W to complete up to 1 year HER2-target therapy inclusive of therapy given both in neoadjuvant & adjuvant setting: placebo 1200 mg IV Q3W, trastuzumab 6 mg/kg IV (with initial 8-mg/kg IV loading dose) Q3W, & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W. Participants who did not achieve pCR had option of receiving blinded atezolizumab + trastuzumab emtansine post surgery for 14 cycles. In response to USM DIL, dated 3 Feb 2021 treatment with placebo was discontinued.

| | |
|---|---|
| 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 was administered by intravenous infusion at a dose of 840 mg Q2W for 4 cycles during neoadjuvant phase followed by placebo 1200 mg IV Q3W for 4 cycles. During the adjuvant phase,

participants continued to receive placebo 1200 mg IV Q3W. In response to USM DIL dated 3 Feb 2021 treatment with placebo must be discontinued.

| | |
|---|---|
| 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 by IV infusion in the neoadjuvant setting at a dosage of 600 mg/m^2 on Day 2 of a 14 day cycle for cylces 1-4.

| | |
|---|---|
| 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 by IV infusion in the neoadjuvant setting at a dosage of 60 mg/m^2 on Day 2 of a 14 day cycle for cylces 1-4.

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

Dosage and administration details:

Paclitaxel was administered by IV infusion in the neoadjuvant setting at a dosage of 80 mg/m^2 for 12 continuous weeks (cycles 5-8).

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

Dosage and administration details:

Trastuzumab was administered on Day 1 of a 21-day cycle as an 8-mg/kg loading dose and then a 6 mg/kg IV Q3W up to 52 weeks.

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

Dosage and administration details:

Pertuzumab was administered on Day 1 of a 21-day cycle as a fixed non-weight-based dose of 840-mg IV loading dose and then 420 mg IV Q3W up to 52 weeks.

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

Dosage and administration details:

Trastuzumab emtansine was administered at a dose of 3.6 mg/kg IV infusion Q3W.

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: The roles blinded are correct

| **Number of subjects in period 1** | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP |
|---|---|---|
| Started | 226 | 228 |
| Completed | 0 | 0 |
| Not completed | 226 | 228 |
| Consent withdrawn by subject | 5 | 5 |
| Physician decision | - | 2 |
| Continuing on Study | 215 | 215 |
| Death | 6 | 4 |
| TSH result is unstable | - | 1 |
| Protocol deviation | - | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Atezolizumab +ddAC-PacHP |

Reporting group description:

Participants received atezolizumab (atezo) 840 mg IV Q2W for 4 cycles during neoadjuvant phase with ddAC (doxorubicin 60 mg/m2 & cyclophosphamide 600 mg/m2 IV), followed by atezo 1200 mg IV Q3W for 4 cycles with paclitaxel 80 mg/m2 IV weekly for 12 continuous weeks, trastuzumab 6 mg/kg IV (with initial 8mg/kg IV loading dose) Q3W for 4 cycles, & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W for 4 cycles. During adjuvant phase, participants continued to receive following study treatments Q3W to complete up to 1 year HER2-target therapy inclusive of therapy given both in neoadjuvant and adjuvant setting: atezo 1200 mg IV Q3W, trastuzumab 6 mg/kg IV (with initial 8-mg/kg IV loading dose) Q3W, & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W. Participants who did not achieve pCR had option of receiving blinded atezo+trastuzumab emtansine post surgery for 14 cycles. In response to USM DIL dated 3 Feb 2021 treatment with atezo was discontinued.

| Reporting group title | Placebo + ddAC-PacHP |
|---|---|

Reporting group description:

Participants received placebo 840 mg IV Q2W for 4 cycles during neoadjuvant phase with ddAC (doxorubicin 60 mg/m2 & cyclophosphamide 600 mg/m2 IV), followed by placebo 1200 mg IV Q3W for 4 cycles with paclitaxel 80 mg/m2 IV weekly for 12 continuous weeks, trastuzumab 6 mg/kg IV (with initial 8-mg/kg IV loading dose) Q3W for 4 cycles & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W for 4 cycles. During adjuvant phase, participants continued to receive following study treatments Q3W to complete up to 1 year HER2-target therapy inclusive of therapy given both in neoadjuvant & adjuvant setting: placebo 1200 mg IV Q3W, trastuzumab 6 mg/kg IV (with initial 8-mg/kg IV loading dose) Q3W, & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W. Participants who did not achieve pCR had option of receiving blinded atezolizumab + trastuzumab emtansine post surgery for 14 cycles. In response to USM DIL, dated 3 Feb 2021 treatment with placebo was discontinued.

| Reporting group values | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | Total |
|---|---|---|---|
| Number of subjects | 226 | 228 | 454 |
| Age Categorical<br>Units: Participants | | | |
| 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) | 204 | 207 | 411 |
| From 65-84 years | 22 | 21 | 43 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 50.3 | 50.8 | |
| standard deviation | ± 10.7 | ± 10.4 | - |
| Sex: Female, Male<br>Units: Participants | | | |
| Male | 1 | 1 | 2 |
| Female | 225 | 227 | 452 |

| Race<br>Units: Subjects | | | |
|---|---|---|---|
| American Indian or Alaska Native | 1 | 1 | 2 |
| Asian | 62 | 66 | 128 |
| Black or African American | 8 | 13 | 21 |
| White | 149 | 142 | 291 |
| Multiple | 2 | 3 | 5 |
| Unknown | 4 | 3 | 7 |
| Ethnicity<br>Units: Subjects | | | |
| Hispanic or Latino | 26 | 33 | 59 |
| Not Hispanic or Latino | 195 | 191 | 386 |
| Not Reported | 5 | 4 | 9 |

## End points

### End points reporting groups

| Reporting group title | Atezolizumab +ddAC-PacHP |
|---|---|

Reporting group description:

Participants received atezolizumab (atezo) 840 mg IV Q2W for 4 cycles during neoadjuvant phase with ddAC (doxorubicin 60 mg/m2 & cyclophosphamide 600 mg/m2 IV), followed by atezo 1200 mg IV Q3W for 4 cycles with paclitaxel 80 mg/m2 IV weekly for 12 continuous weeks, trastuzumab 6 mg/kg IV (with initial 8mg/kg IV loading dose) Q3W for 4 cycles, & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W for 4 cycles. During adjuvant phase, participants continued to receive following study treatments Q3W to complete up to 1 year HER2-target therapy inclusive of therapy given both in neoadjuvant and adjuvant setting: atezo 1200 mg IV Q3W, trastuzumab 6 mg/kg IV (with initial 8-mg/kg IV loading dose) Q3W, & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W. Participants who did not achieve pCR had option of receiving blinded atezo+trastuzumab emtansine post surgery for 14 cycles. In response to USM DIL dated 3 Feb 2021 treatment with atezo was discontinued.

| Reporting group title | Placebo + ddAC-PacHP |
|---|---|

Reporting group description:

Participants received placebo 840 mg IV Q2W for 4 cycles during neoadjuvant phase with ddAC (doxorubicin 60 mg/m2 & cyclophosphamide 600 mg/m2 IV), followed by placebo 1200 mg IV Q3W for 4 cycles with paclitaxel 80 mg/m2 IV weekly for 12 continuous weeks, trastuzumab 6 mg/kg IV (with initial 8-mg/kg IV loading dose) Q3W for 4 cycles & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W for 4 cycles. During adjuvant phase, participants continued to receive following study treatments Q3W to complete up to 1 year HER2-target therapy inclusive of therapy given both in neoadjuvant & adjuvant setting: placebo 1200 mg IV Q3W, trastuzumab 6 mg/kg IV (with initial 8-mg/kg IV loading dose) Q3W, & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W. Participants who did not achieve pCR had option of receiving blinded atezolizumab + trastuzumab emtansine post surgery for 14 cycles. In response to USM DIL, dated 3 Feb 2021 treatment with placebo was discontinued.

### Primary: Percentage of Participants with Pathological Complete Response (pCR) in the PD-L1-Positive Population (IC 1/2/3)

| End point title | Percentage of Participants with Pathological Complete Response (pCR) in the PD-L1-Positive Population (IC 1/2/3) |
|---|---|

End point description:

pCR is defined as the absence of residual invasive cancer on hematoxylin and eosin evaluation of the complete resected breast specimen and all sampled regional lymph nodes following completion of neoadjuvant systemic therapy (NAST) (i.e., ypT0/is ypN0 in the current American Joint Committee on Cancer [AJCC] staging system, 8th edition). The PD-L1-positive population is defined as participants in the Intent-to-Treat (ITT) population whose PD-L1 status is IC1/2/3 at the time of randomization.

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

End point timeframe:

From randomization to approximately 6 months

| End point values | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 109 | 109 | | |
| Units: Percentage of Particpants | | | | |
| number (not applicable) | 64.2 | 72.5 | | |

## Statistical analyses

| Statistical analysis title | Atezolizumab +ddAC-PacHP vs. Placebo + ddAC-PacHP |
|---|---|

Statistical analysis description:

Treatment comparison was made using Cochran-Mantel-Haenszel test stratified by disease stage (T2 vs. T3-4) and hormone receptor status (estrogen receptor (ER) positive and/or progesterone receptor (PgR) positive vs. ER negative and PgR negative).

| | |
|---|---|
| Comparison groups | Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP |
| Number of subjects included in analysis | 218 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.1846 [1] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.67 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.37 |
| upper limit | 1.21 |

Notes:

[1] - The threshold for statistical significance was a p-value =0.048

## Primary: pCR in the ITT Population

| End point title | pCR in the ITT Population |
|---|---|

End point description:

pCR is defined as the absence of residual invasive cancer on hematoxylin and eosin evaluation of the complete resected breast specimen and all sampled regional lymph nodes following completion of neoadjuvant systemic therapy (NAST) (i.e., ypT0/is ypN0 in the current American Joint Committee on Cancer [AJCC] staging system, 8th edition). The ITT population is defined as all randomized participants, regardless of whether the assigned study treatment was received.

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

End point timeframe:

From randomization to approximately 6 months

| End point values | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 226 | 228 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 62.4 | 62.7 | | |

## Statistical analyses

| Statistical analysis title | Atezolizumab +ddAC-PacHP vs. Placebo + ddAC-PacHP |
|---|---|

Statistical analysis description:

Treatment comparison was made using Cochran-Mantel-Haenszel test stratified by disease stage (T2 vs. T3-4) and hormone receptor status (ER positive and/or PgR positive vs. ER negative and PgR negative).

| | |
|---|---|
| Comparison groups | Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP |

| | |
|---|---|
| Number of subjects included in analysis | 454 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9551 [2] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.99 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.67 |
| upper limit | 1.46 |

Notes:

[2] - The threshold for statistical significance was a p-value =0.002

## Secondary: Percentage of Participants with pCR Based on Hormone Receptor Status

| | |
|---|---|
| End point title | Percentage of Participants with pCR Based on Hormone Receptor Status |

End point description:

pCR (ypT0/is ypN0) based upon hormone receptor status (estrogen receptor [ER]/progesterone receptor [PgR] positive or ER/PgR negative). The ITT population is defined as all randomized participants, regardless of whether the assigned study treatment was received.

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

End point timeframe:

From randomization to approximately 24 months.

| End point values | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 226 | 228 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| ER+ and/or PgR+ (n= 116, 117) | 50.9 | 54.7 | | |
| ER- and/or PgR- (n= 110, 111) | 74.5 | 71.2 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with pCR in the PD-L1-Negative Population

| | |
|---|---|
| End point title | Percentage of Participants with pCR in the PD-L1-Negative Population |

End point description:

pCR (ypT0/is ypN0) in the IC 0 Population. The PD-L1-negative population is defined as participants in the ITT population whose PD-L1 status is IC 0 at the time of randomization.

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

End point timeframe:

From randomization to approximately 24 months

| End point values | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 117 | 119 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 60.7 | 53.8 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Event-Free Survival (EFS)

| End point title | Event-Free Survival (EFS) |
|---|---|

End point description:

EFS defined as the time from randomization to the first documented disease recurrence, unequivocal tumor progression determined by the treating investigator, or death from any cause, whichever occurs first, in all patients and based upon hormone receptor status (ER/PgR positive or ER/PgR negative) and PD-L1 status (IC 0; IC 1/2/3). The ITT population is defined as all randomized participants, regardless of whether the assigned study treatment was received. Data collection is still ongoing and the results will be disclosed within 1 year from the Study Completion Date.

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

End point timeframe:

From randomization to first documented disease recurrence, unequivocal tumor progression determined by the treating investigator, or death from any cause (up to approximately 54 months)

| End point values | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[3] | 0[4] | | |
| Units: Months | | | | |
| median (confidence interval 95%) | ( to ) | ( to ) | | |

Notes:

[3] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[4] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

### 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 defined as the time from surgery to the first documented disease recurrence or death from any

cause, whichever occurs first, in all patients who undergo surgery and based upon hormone receptor status (ER/PgR positive or ER/PgR negative) and PD-L1 status (IC 0; IC 1/2/3). The ITT population is defined as all randomized participants, regardless of whether the assigned study treatment was received. Data collection is still ongoing and the results will be disclosed within 1 year from the Study Completion Date.

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

End point timeframe:

Time from surgery to first documented disease recurrence or death from any cause (up to approximately 54 months)

| **End point values** | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[5] | 0[6] | | |
| Units: Months | | | | |
| median (confidence interval 95%) | ( to ) | ( to ) | | |

Notes:

[5] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[6] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

### Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Survival (OS)

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

End point description:

OS defined as the time from randomization to death from any cause in all patients and based upon hormone receptor status (ER/PgR positive or ER/PgR negative) and PD-L1 status (IC 0; IC 1/2/3). The ITT population is defined as all randomized participants, regardless of whether the assigned study treatment was received. Data collection is still ongoing and the results will be disclosed within 1 year from the Study Completion Date.

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

End point timeframe:

From randomization to date of death from any cause (up to approximately 54 months)

| **End point values** | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[7] | 0[8] | | |
| Units: Months | | | | |
| median (confidence interval 95%) | ( to ) | ( to ) | | |

Notes:

[7] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[8] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

### Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Changes From Baseline in Function (Role, Physical)

| End point title | Mean Changes From Baseline in Function (Role, Physical) |
|---|---|

End point description:

EORTC QLQ-C30 is a self-reported questionnaire that included functional scales (physical, role, cognitive, emotional, social), symptom scales (fatigue, pain, nausea/vomiting), global health scale/quality of life (GHS/QOL) and single items (dyspnea, appetite loss, insomnia, constipation, diarrhea, financial difficulties). Questions 1-28 on the QLQ-C30 were on a 4-point scale (1=Not at All to 4=Very Much). Questions 29-30 (GHS scale) were on a 7-point scale (1=Very Poor to 7=Excellent). For this instrument, GHS/QOL and functional scales were linearly transformed so each score ranged 0-100, where lower scores indicate poorer functioning (e.g., worsening) and higher scores indicate better functioning (e.g., improvement). The patient-reported outcomes (PRO)-evaluable population is defined as participants in the ITT population with a baseline and at least 1 post-baseline PRO assessment. 9999999 = SD was non-estimable as only 1 participant was evaluated for this category.

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

End point timeframe:

Baseline; Day 1 of Cycle 1-9, on Day 1 of every other cycle thereafter until Cycle 22; at the treatment discontinuation or early termination visit and follow up visit. Cycle 1-4, each cycle is 14 days. Cycle 5-22, each cycle is 21 days.

| **End point values** | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 223 | 224 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Role: Baseline (n=223, 224) | 91.70 (± 16.28) | 90.85 (± 20.26) | | |
| Role: Cycle (C) 2 Day (D) 1 (n=222, 222) | -13.06 (± 23.02) | -9.83 (± 23.08) | | |
| Role: C3D1 (n=219, 220) | -17.88 (± 26.20) | -15.15 (± 22.64) | | |
| Role: C4D1 (n=217, 216) | -22.27 (± 27.04) | -17.98 (± 25.10) | | |
| Role: C5D1 (n=218, 219) | -24.08 (± 28.21) | -19.79 (± 26.36) | | |
| Role: C6D1 (n=215, 216) | -20.70 (± 25.46) | -18.60 (± 25.01) | | |
| Role: C7D1 (n=210, 210) | -19.21 (± 25.50) | -16.67 (± 26.34) | | |
| Role: C8D1 (n=211, 208) | -21.25 (± 26.48) | -17.79 (± 26.39) | | |
| Role: Adjuvant Week 1 D1 (n=206, 202) | -22.82 (± 26.70) | -26.24 (± 31.27) | | |
| Role: Adjuvant Week 7 D43 (n=183, 176) | -15.48 (± 22.31) | -15.15 (± 26.50) | | |
| Role: Adjuvant Week 13 D85 (n=171, 163) | -14.42 (± 23.77) | -15.24 (± 26.99) | | |
| Role: Adjuvant Week 19 D127 (n=155, 147) | -14.30 (± 24.26) | -15.42 (± 25.74) | | |
| Role: Adjuvant Week 25 D169 (n=134, 127) | -13.68 (± 24.00) | -15.88 (± 22.99) | | |
| Role: Adjuvant Week 31 D211 (n=112, 110) | -13.24 (± 23.69) | -14.55 (± 24.43) | | |
| Role: Adjuvant Week 37 D253 (n=91, 94) | -9.34 (± 21.11) | -15.43 (± 27.35) | | |
| Role: End of Treatment (EOT) (n=108, 116) | -14.04 (± 25.18) | -18.10 (± 29.04) | | |

| | | | | |
|---|---|---|---|---|
| Role: Follow-Up (FU) 1 D1 (n=62, 68) | -11.02 (± 25.06) | -17.16 (± 23.21) | | |
| Role: FU2D92 (n=20, 33) | -9.17 (± 23.24) | -14.65 (± 25.94) | | |
| Role: FU3D183 (n=3, 8) | -16.67 (± 16.67) | -10.42 (± 21.71) | | |
| Role: FU4D274 (n=3, 6) | -27.78 (± 25.46) | -25.00 (± 9.13) | | |
| Role: FU5D457 (n=0, 1) | 0.0 (± 0.0) | -33.33 (± 9999999) | | |
| Physical: Baseline (n=223, 224) | 92.74 (± 11.60) | 92.20 (± 12.92) | | |
| Physical: C2D1 (n=222, 221) | -4.32 (± 9.75) | -3.88 (± 13.44) | | |
| Physical: C3D1 (n=219, 220) | -6.82 (± 13.39) | -7.18 (± 12.91) | | |
| Physical: C4D1 (n=217, 216) | -11.98 (± 17.67) | -9.48 (± 14.65) | | |
| Physical: C5D1 (n=218, 219) | -12.84 (± 18.19) | -10.67 (± 15.91) | | |
| Physical: C6D1 (n=215, 216) | -12.25 (± 15.97) | -11.40 (± 17.05) | | |
| Physical: C7D1 (n=210, 210) | -11.33 (± 14.86) | -11.45 (± 17.43) | | |
| Physical: C8D1 (n=211, 208) | -13.30 (± 17.11) | -11.56 (± 17.54) | | |
| Physical: Adjuvant Week 1 D1 (n=206, 202) | -12.27 (± 18.26) | -12.19 (± 19.27) | | |
| Physical: Adjuvant Week 7 D43 (n=183, 176) | -8.96 (± 14.74) | -8.60 (± 16.33) | | |
| Physical: Adjuvant Week 13 D85 (n=171, 163) | -8.38 (± 14.97) | -8.88 (± 15.04) | | |
| Physical: Adjuvant Week 19 D127 (n=154, 147) | -9.22 (± 15.17) | -10.03 (± 15.52) | | |
| Physical: Adjuvant Week 25 D169 (n=134, 127) | -9.35 (± 16.19) | -8.45 (± 14.34) | | |
| Physical: Adjuvant Week 31 D211 (n=112, 110) | -7.80 (± 13.69) | -9.88 (± 15.84) | | |
| Physical: Adjuvant Week 37 D253 (n=91, 94) | -7.77 (± 13.67) | -10.78 (± 16.82) | | |
| EOT (n=109, 116) | -8.20 (± 15.78) | -13.05 (± 19.17) | | |
| Physical: FU1D1 (n=62, 68) | -8.06 (± 18.11) | -11.57 (± 19.29) | | |
| Physical: FU2D92 (n=20, 33) | -3.33 (± 12.52) | -9.90 (± 15.73) | | |
| Physical: FU3D183 (n=3, 8) | 2.22 (± 16.78) | -14.17 (± 7.51) | | |
| Physical: FU4D274 (n=3, 6) | 0.00 (± 20.00) | -6.67 (± 11.93) | | |
| Physical: FU5D457 (n=0, 1) | 0.0 (± 0.0) | 60.00 (± 9999999) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Changes From Baseline in Global Health Status

| End point title | Mean Changes From Baseline in Global Health Status |
|---|---|

End point description:

EORTC QLQ-C30 is a self-reported questionnaire that included functional scales (physical, role, cognitive, emotional, social), symptom scales (fatigue, pain, nausea/vomiting), GHS/QOL and single items (dyspnea, appetite loss, insomnia, constipation, diarrhea, financial difficulties). Questions 1-28 on the QLQ-C30 were on a 4-point scale (1=Not at All to 4=Very Much). Questions 29-30 (GHS scale) were on a 7-point scale (1=Very Poor to 7=Excellent). For this instrument, GHS/QOL and functional scales were linearly transformed so each score ranged 0-100, where lower scores indicate poorer functioning (e.g., worsening) and higher scores indicate better functioning (e.g., improvement). The PRO-evaluable population is defined as participants in the ITT population with a baseline and at least 1 post-baseline PRO assessment. 9999999 = SD was non-estimable as only 1 participant was evaluated for this category.

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

End point timeframe:

Baseline; Day 1 of Cycle 1-9, on Day 1 of every other cycle thereafter until Cycle 22; at the treatment discontinuation or early termination visit and follow up visit. Cycle 1-4, each cycle is 14 days. Cycle 5-22, each cycle is 21 days.

| **End point values** | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 223 | 224 | | |
| Units: Units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=223, 224) | 76.49 (± 19.33) | 76.79 (± 19.05) | | |
| C2D1 (n=222, 222) | -7.28 (± 19.70) | -6.31 (± 19.54) | | |
| C3D1 (n=219, 220) | -10.96 (± 22.16) | -8.33 (± 20.93) | | |
| C4D1 (n=217, 216) | -13.67 (± 22.47) | -10.88 (± 21.51) | | |
| C5D1 (n=218, 219) | -14.14 (± 23.76) | -12.63 (± 23.66) | | |
| C6D1 (n=215, 216) | -12.33 (± 22.10) | -9.99 (± 20.96) | | |
| C7D1 (n=210, 210) | -11.47 (± 19.81) | -10.52 (± 21.59) | | |
| C8D1 (n=211, 208) | -12.72 (± 22.45) | -10.86 (± 22.66) | | |
| Adjuvant Week 1 D1 (n=206, 202) | -7.89 (± 21.89) | -7.14 (± 23.68) | | |
| Adjuvant Week 7 D43 (n=183, 176) | -7.51 (± 22.97) | -5.21 (± 21.96) | | |
| Adjuvant Week 13 D85 (n=171, 163) | -7.07 (± 22.31) | -6.75 (± 21.13) | | |
| Adjuvant Week 19 D127 (n=155, 147) | -7.20 (± 21.47) | -6.01 (± 20.52) | | |
| Adjuvant Week 25 D169 (n=134, 127) | -8.02 (± 21.10) | -5.05 (± 20.39) | | |
| Adjuvant Week 31 D211 (n=112, 110) | -7.29 (± 21.75) | -7.80 (± 22.56) | | |
| Adjuvant Week 37 D253 (n=91, 94) | -5.95 (± 21.71) | -6.03 (± 20.72) | | |
| EOT (n=109, 116) | -5.96 (± 22.08) | -9.41 (± 24.29) | | |
| FU1D1 (n=62, 68) | -3.90 (± 21.64) | -5.15 (± 21.01) | | |

| | | | | |
|---|---|---|---|---|
| FU2D92 (n=20, 33) | -1.25 (± 19.55) | -3.03 (± 16.11) | | |
| FU3D183 (n=3, 8) | -8.33 (± 8.33) | -7.29 (± 15.06) | | |
| FU4D274 (n=3, 6) | -13.89 (± 12.73) | -31.94 (± 37.42) | | |
| FU5D457 (n=0, 1) | 0.0 (± 0.0) | -16.67 (± 9999999) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants With Adverse Events

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

End point description:

The safety-evaluable population is defined as participants who received at least one dose of any study drug.

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

End point timeframe:

From randomization up until clinical cut-off date (approximately 24 months)

| End point values | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 226 | 225 | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 100 | 100 | | |

### Statistical analyses

No statistical analyses for this end point

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

| End point title | Maximum Serum Concentration (Cmax) of Atezolizumab[9] |
|---|---|

End point description:

Cmax is the maximum (or peak) concentration that a study drug achieves in the body. The pharmacokinetic (PK)-evaluable population is defined as all participants who received any dose of study medication and who have at least one post-baseline PK sample available.

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

End point timeframe:

30 minutes post infusion on Day 1 Cycle (C) 1.

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 analyses for this end point. Atezolizumab was not administered in the placebo arm.

| End point values | Atezolizumab +ddAC-PacHP | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 219 | | | |
| Units: micrograms/milliliters (ug/mL) | | | | |
| arithmetic mean (standard deviation) | 348 (± 122) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Minimum Serum Concentration (Cmin) of Atezolizumab

| End point title | Minimum Serum Concentration (Cmin) of Atezolizumab[10] |
|---|---|

End point description:

Cmin is the minimum (or trough) concentration that a study drug achieves in the body. The PK-evaluable population is defined as all participants who received any dose of study medication and who have at least one post-baseline PK sample available.

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

End point timeframe:

Pre-dose on Day 1 Cycle (C) 2, 3, 4, 8, 12, 16, ATDV (an average of 1 year). C 2-4, each C is 14 days. C 8-16, each C is 21 days. With protocol version 5, collection is only required ATDV/completion (an average of 1 year).

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 analyses for this end point. Atezolizumab was not administered in the placebo arm.

| End point values | Atezolizumab +ddAC-PacHP | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 226 | | | |
| Units: ug/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| C2D1/predose (n=222) | 103 (± 40.3) | | | |
| C3D1/predose (n=214) | 163 (± 44.4) | | | |
| C4D1/predose (n=212) | 204 (± 51.9) | | | |
| C8D1/predose (n=203) | 225 (± 97.1) | | | |
| C12D1/predose (n=166) | 217 (± 101) | | | |
| C16D1/predose (n=133) | 226 (± 114) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Trough Concentration (Ctrough) for Pertuzumab and Trastuzumab in Serum

| End point title | Trough Concentration (Ctrough) for Pertuzumab and Trastuzumab in Serum |
|---|---|

End point description:

The PK-evaluable population is defined as all participants who received any dose of study medication and who have at least one post-baseline PK sample available.

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

End point timeframe:

Pre-dose on Day 1 Cycle (C) 8, 12, and at treatment discontinuation visit (ATDV) (an average of 1 year). C 1-4, each C is 14 days. C 8-12, each C is 21 days. With protocol version 5, collection is only required ATDV/completion (an average of 1 year).

| **End point values** | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 226 | 225 | | |
| Units: ug/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pertuzumab: C8D1/predose (n=205, 201) | 93.2 (± 40.7) | 94.8 (± 39.8) | | |
| Pertuzumab: C12D1/predose (n=150, 147) | 87.7 (± 58.4) | 91.6 (± 59.7) | | |
| Trastuzumab: C8D1/predose (n=205, 201) | 58.5 (± 29.1) | 56.5 (± 23.9) | | |
| Trastuzumab: C12D1/predose (n=150, 147) | 62.4 (± 32.7) | 60.4 (± 30.9) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Cmin of Trastuzumab Emtansine in Serum

| End point title | Cmin of Trastuzumab Emtansine in Serum |
|---|---|

End point description:

Cmin is the minimum (or trough) concentration that a study drug achieves in the body. The PK-evaluable population is defined as all participants who received any dose of study medication and who have at least one post-baseline PK sample available. Data collection is still ongoing and the results will be disclosed within 1 year from the Study Completion Date.

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

End point timeframe:

Pre-dosDay 1 of Cycle 9 and Cycle 12, at treatment disontinuation visit (an average of 1 year). Cycle 9 and 12 are each 21 days. With protocol version 5, collection is only required at the time of treatment discontinuation/completion (an average of 1 year

| **End point values** | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[11] | 0[12] | | |
| Units: ug/mL | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[11] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[12] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

### Statistical analyses

No statistical analyses for this end point

### Secondary: Cmax of Trastuzumab Emtansine in Serum

| End point title | Cmax of Trastuzumab Emtansine in Serum |
|---|---|

End point description:

Cmax is the maximum (or peak) concentration that a study drug achieves in the body. The PK-evaluable population is defined as all participants who received any dose of study medication and who have at least one post-baseline PK sample available. Data collection is still ongoing and the results will be disclosed within 1 year from the Study Completion Date.

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

End point timeframe:

Day 1 of Cycle 9 and Cycle 12, at treatment disontinuation visit (an average of 1 year). Cycle 9 and 12 are each 21 days. With protocol version 5, collection is only required at the time of treatment discontinuation/completion (an average of 1 year).

| End point values | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[13] | 0[14] | | |
| Units: ug/mL | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[13] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[14] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Treatment-Emergent Anti-Drug Antibodies (ADAs) to Atezolizumab

| End point title | Number of Participants with Treatment-Emergent Anti-Drug Antibodies (ADAs) to Atezolizumab[15] |
|---|---|

End point description:

Participants were considered to be treatment-emergent ADA-positive if they were ADA-negative or had missing data at baseline but developed an ADA response following study drug exposure (treatment-induced ADA response), or if they were ADA-positive at baseline and the titer of one or more post-baseline samples was at least 0.60 titer units greater than the titer of the baseline sample (treatment-enhanced ADA response). Participants were considered to be treatment-emergent ADA-negative if they were ADA-negative or were missing data at baseline and all post-baseline samples were negative, or if they were ADA-positive at baseline but did not have any post-baseline samples with a titer that was at least 0.60 titer units greater than the titer of the baseline sample (treatment unaffected). The immunogenicity analysis included all safety evealuable participants who had at least one baseline or post-baseline ADA result from at least one sample.

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

End point timeframe:

Day 1 Cycle (C) 1, 2, 3, 4, 8, 12, 16, at treatment discontinuation visit (ATDV) (an average of 1 year). C 1-4, each C is 14 days. C 8-16, each C is 21 days. With protocol version 5, collection is only required ATDV/completion (an average of 1 year).

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point. Atezolizumab was not administered in the placebo arm.

| **End point values** | Atezolizumab +ddAC-PacHP | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 225 | | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Baseline (BL): ADA Positive | 1 | | | |
| BL: ADA Negative | 224 | | | |
| Post-BL: Treatment-Emergent ADA Positive | 7 | | | |
| Post-BL: Treatment-Emergent ADA Negative | 218 | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Treatment-Emergent ADAs to Trastuzumab

| End point title | Number of Participants with Treatment-Emergent ADAs to Trastuzumab |
|---|---|

End point description:

Participants were considered to be treatment-emergent ADA-positive if they were ADA-negative or had missing data at baseline but developed an ADA response following study drug exposure (treatment-induced ADA response), or if they were ADA-positive at baseline and the titer of one or more post-baseline samples was at least 0.60 titer units greater than the titer of the baseline sample (treatment-enhanced ADA response). Participants were considered to be treatment-emergent ADA-negative if they were ADA-negative or were missing data at baseline and all post-baseline samples were negative, or if they were ADA-positive at baseline but did not have any post-baseline samples with a titer that was at least 0.60 titer units greater than the titer of the baseline sample (treatment unaffected). The immunogenicity analysis included all safety evealuable participants who had at least one baseline or post-baseline ADA result from at least one sample.

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

End point timeframe:

Day 1 Cycle (C) 1, 8, 12 and at treatment discontinuation visit (ATDV) (an average of 1 year). C 1-4, each C is 14 days. C 8-12, each C is 21 days. With protocol version 5, collection is only required ATDV/completion (an average of 1 year).

| End point values | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 225 | 225 | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| BL: ADA Positive (n=220, 211) | 2 | 1 | | |
| BL: ADA Negative (220, 211) | 218 | 210 | | |
| Post-BL: Trt.-Emergent ADA Positive (n=216, 214) | 1 | 0 | | |
| Post-BL: Trt.-Emergent ADA Negative (n=216, 214) | 215 | 214 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Treatment-Emergent ADAs to Pertuzumab

| End point title | Number of Participants with Treatment-Emergent ADAs to Pertuzumab |
|---|---|

End point description:

Participants were considered to be treatment-emergent ADA-positive if they were ADA-negative or had missing data at baseline but developed an ADA response following study drug exposure (treatment-induced ADA response), or if they were ADA-positive at baseline and the titer of one or more post-baseline samples was at least 0.60 titer units greater than the titer of the baseline sample (treatment-enhanced ADA response). Participants were considered to be treatment-emergent ADA-negative if they were ADA-negative or were missing data at baseline and all post-baseline samples were negative, or if they were ADA-positive at baseline but did not have any post-baseline samples with a titer that was at least 0.60 titer units greater than the titer of the baseline sample (treatment unaffected). The immunogenicity analysis included all safety evealuable participants who had at least one baseline or post-baseline ADA result from at least one sample.

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

End point timeframe:

Day 1 of Cycle (C) 1, 8, 12, and at treatment discontinuation visit (ATDV) (an average of 1 year). C 1-4, each C is 14 days. C 8-12, each C is 21 days. With protocol version 5, collection is only required ATDV/completion (an average of 1 year).

| End point values | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 225 | 225 | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| BL: ADA Positive (n=221, 211) | 6 | 3 | | |
| BL: ADA Negative (n=221, 211) | 215 | 208 | | |
| Post-BL: Trt-Emergent ADA Positive (n=216, 214) | 13 | 12 | | |
| Post-BL: Trt-Emergent ADA Negative (n=216, 214) | 203 | 202 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Particpants with pCR Based on PIK3CA Mutation Status

| End point title | Percentage of Particpants with pCR Based on PIK3CA Mutation Status |
|---|---|

End point description:

pCR is defined as the absence of residual invasive cancer on hematoxylin and eosin evaluation of the complete resected breast specimen and all sampled regional lymph nodes following completion of neoadjuvant systemic therapy (NAST) (i.e., ypT0/is ypN0 in the current American Joint Committee on Cancer [AJCC] staging system, 8th edition). The ITT population is defined as all randomized participants, regardless of whether the assigned study treatment was received.

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

End point timeframe:

From randomization to approximately 24 months

| End point values | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 226 | 228 | | |
| Units: Percentage of participants with pCR | | | | |
| number (not applicable) | | | | |
| Mutated (n pCR=40, 34) | 59.7 | 55.7 | | |
| Wildtype (n pCR=98, 101) | 65.3 | 65.2 | | |
| Missing (n pCR=3, 8) | 33.3 | 66.7 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Treatment-Emergent ADAs to Trastuzumab Emtansine

| End point title | Number of Participants with Treatment-Emergent ADAs to Trastuzumab Emtansine |
|---|---|

End point description:

Participants were considered to be treatment-emergent ADA-positive if they were ADA-negative or had missing data at baseline but developed an ADA response following study drug exposure (treatment-induced ADA response), or if they were ADA-positive at baseline and the titer of one or more post-baseline samples was at least 0.60 titer units greater than the titer of the baseline sample (treatment-enhanced ADA response). Participants were considered to be treatment-emergent ADA-negative if they were ADA-negative or were missing data at baseline and all post-baseline samples were negative, or if they were ADA-positive at baseline but did not have any post-baseline samples with a titer that was at

least 0.60 titer units greater than the titer of the baseline sample (treatment unaffected). Data collection is still ongoing and the results will be disclosed within 1 year from the Study Completion Date.

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

End point timeframe:

Day 1 of Cycle 9 and Cycle 12, at treatment disontinuation visit (an average of 1 year). Cycle 9 and 12 are each 21 days. With protocol version 5, collection is only required at the time of treatment discontinuation/completion (an average of 1 year).

| **End point values** | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[16] | 0[17] | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |

Notes:

[16] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[17] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

### Statistical analyses

No statistical analyses for this end point

## Secondary: EFS Based on PIK3CA Mutation Status

| End point title | EFS Based on PIK3CA Mutation Status |
|---|---|

End point description:

Data collection is still ongoing and the results will be disclosed within 1 year from the Study Completion Date.

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

End point timeframe:

From randomization to first documented disease recurrence, unequivocal tumor progression determined by the treating investigator, or death from any cause (up to approximately 54 months)

| **End point values** | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[18] | 0[19] | | |
| Units: Months | | | | |
| median (confidence interval 95%) | ( to ) | ( to ) | | |

Notes:

[18] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[19] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

### Statistical analyses

No statistical analyses for this end point

## Secondary: DFS Based on PIK3CA Mutation Status

| End point title | DFS Based on PIK3CA Mutation Status |
|---|---|

End point description:

Data collection is still ongoing and the results will be disclosed within 1 year from the Study Completion Date.

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

End point timeframe:

Time from surgery to first documented disease recurrence or death from any cause (up to approximately 54 months)

| **End point values** | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[20] | 0[21] | | |
| Units: Months | | | | |
| median (confidence interval 95%) | ( to ) | ( to ) | | |

Notes:

[20] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[21] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

### Statistical analyses

No statistical analyses for this end point

## Secondary: OS Based on PIK3CA Mutation Status

| End point title | OS Based on PIK3CA Mutation Status |
|---|---|

End point description:

Data collection is still ongoing and the results will be disclosed within 1 year from the Study Completion Date.

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

End point timeframe:

From randomization to date of death from any cause (up to approximately 54 months)

| **End point values** | Atezolizumab +ddAC-PacHP | Placebo + ddAC-PacHP | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 0[22] | 0[23] | | |
| Units: Months | | | | |
| median (confidence interval 95%) | ( to ) | ( to ) | | |

Notes:

[22] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

[23] - Data collection is ongoing and the results will be disclosed within 1 year from Study Completion

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline up until clinical cut off date (approximately 24 months)

Adverse event reporting additional description:

AEs were recorded for the safety-evaluable population which included all randomized participants who received any dose of study drug.

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

### Dictionary used

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

### Reporting groups

| | |
|---|---|
| Reporting group title | Placebo + ddAC-PacHP |

Reporting group description:

Participants received placebo 840 mg IV Q2W for 4 cycles during neoadjuvant phase with ddAC (doxorubicin 60 mg/m2 & cyclophosphamide 600 mg/m2 IV), followed by placebo 1200 mg IV Q3W for 4 cycles with paclitaxel 80 mg/m2 IV weekly for 12 continuous weeks, trastuzumab 6 mg/kg IV (with initial 8-mg/kg IV loading dose) Q3W for 4 cycles & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W for 4 cycles. During adjuvant phase, participants continued to receive following study treatments Q3W to complete up to 1 year HER2-target therapy inclusive of therapy given both in neoadjuvant & adjuvant setting: placebo 1200 mg IV Q3W, trastuzumab 6 mg/kg IV (with initial 8-mg/kg IV loading dose) Q3W, & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W. Participants who did not achieve pCR had option of receiving blinded atezolizumab + trastuzumab emtansine post surgery for 14 cycles. In response to USM DIL, dated 3 Feb 2021 treatment with placebo was discontinued.

| | |
|---|---|
| Reporting group title | Atezolizumab +ddAC-PacHP |

Reporting group description:

Participants received atezolizumab (atezo) 840 mg IV Q2W for 4 cycles during neoadjuvant phase with ddAC (doxorubicin 60 mg/m2 & cyclophosphamide 600 mg/m2 IV), followed by atezo 1200 mg IV Q3W for 4 cycles with paclitaxel 80 mg/m2 IV weekly for 12 continuous weeks, trastuzumab 6 mg/kg IV (with initial 8mg/kg IV loading dose) Q3W for 4 cycles, & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W for 4 cycles. During adjuvant phase, participants continued to receive following study treatments Q3W to complete up to 1 year HER2-target therapy inclusive of therapy given both in neoadjuvant and adjuvant setting: atezo 1200 mg IV Q3W, trastuzumab 6 mg/kg IV (with initial 8-mg/kg IV loading dose) Q3W, & pertuzumab 420 mg IV (with initial 840-mg IV loading dose) Q3W. Participants who did not achieve pCR had option of receiving blinded atezo+trastuzumab emtansine post surgery for 14 cycles. In response to USM DIL dated 3 Feb 2021 treatment with atezo was discontinued.

| **Serious adverse events** | Placebo + ddAC-PacHP | Atezolizumab +ddAC-PacHP | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 44 / 225 (19.56%) | 62 / 226 (27.43%) | |
| number of deaths (all causes) | 4 | 6 | |
| number of deaths resulting from adverse events | 0 | 2 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| MENINGIOMA | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| NERVOUS SYSTEM NEOPLASM BENIGN | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| SUBCLAVIAN VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 2 / 226 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DEEP VEIN THROMBOSIS | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| THROMBOSIS | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VASCULAR PAIN | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| JUGULAR VEIN THROMBOSIS | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| 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 | | | |
| PYREXIA | | | |
| subjects affected / exposed | 3 / 225 (1.33%) | 3 / 226 (1.33%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FATIGUE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| 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 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CAPSULAR CONTRACTURE ASSOCIATED WITH BREAST IMPLANT | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Reproductive system and breast disorders** | | | |
| ADNEXAL TORSION | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Respiratory, thoracic and mediastinal disorders** | | | |
| DYSPNOEA EXERTIONAL | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INTERSTITIAL LUNG DISEASE | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ALVEOLITIS | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| IMMUNE-MEDIATED PNEUMONITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DYSPNOEA | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONITIS | | | |
| subjects affected / exposed | 2 / 225 (0.89%) | 9 / 226 (3.98%) | |
| occurrences causally related to treatment / all | 2 / 2 | 9 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ACUTE RESPIRATORY DISTRESS SYNDROME | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 3 / 225 (1.33%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 2 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| DEPRESSION | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |
| DEVICE EXTRUSION | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Investigations | | | |
| GAMMA-GLUTAMYLTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GLYCOSYLATED HAEMOGLOBIN INCREASED | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LIPASE INCREASED | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TRANSAMINASES INCREASED | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| EJECTION FRACTION DECREASED | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| WHITE BLOOD CELL COUNT DECREASED | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OXYGEN SATURATION DECREASED | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| IMPLANTATION COMPLICATION | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| WOUND COMPLICATION | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SEROMA | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LUMBAR VERTEBRAL FRACTURE | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RADIATION PNEUMONITIS | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INFUSION RELATED REACTION | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| ATRIAL TACHYCARDIA | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| CARDIAC FAILURE CHRONIC | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MITRAL VALVE INCOMPETENCE | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC FAILURE ACUTE | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC FAILURE CONGESTIVE | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SUPRAVENTRICULAR TACHYCARDIA | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC FAILURE | | | |
| subjects affected / exposed | 5 / 225 (2.22%) | 3 / 226 (1.33%) | |
| occurrences causally related to treatment / all | 6 / 6 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| MENINGITIS NONINFECTIVE | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|---|---|---|
| NEUTROPENIA | | | |
| subjects affected / exposed | 2 / 225 (0.89%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 3 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ANAEMIA | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FEBRILE NEUTROPENIA | | | |
| subjects affected / exposed | 3 / 225 (1.33%) | 10 / 226 (4.42%) | |
| occurrences causally related to treatment / all | 3 / 3 | 11 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LEUKOPENIA | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| APLASTIC ANAEMIA | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| MEIBOMIANITIS | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| EYE DISCHARGE | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| COLITIS | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| DIARRHOEA | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| IMMUNE-MEDIATED PANCREATITIS | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NAUSEA | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 2 / 226 (0.88%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| STOMATITIS | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PANCREATITIS | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| HEPATIC HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| STEATOHEPATITIS | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPERTRANSAMINASAEMIA | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BILIARY COLIC | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 2 / 226 (0.88%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| SECONDARY ADRENOCORTICAL INSUFFICIENCY | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| 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 / 225 (0.00%) | 4 / 226 (1.77%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPOPHYSITIS | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPOTHYROIDISM | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| POST PROCEDURAL INFECTION | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (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 | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| PNEUMOCYSTIS JIROVECII PNEUMONIA | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VULVAL CELLULITIS | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VASCULAR ACCESS SITE INFECTION | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 2 / 226 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| ABSCESS | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BACTERAEMIA | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FEBRILE INFECTION | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| APPENDICITIS | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MASTITIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 225 (0.00%) | 2 / 226 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 2 / 226 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA BACTERIAL | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| 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 | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ANAL ABSCESS | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SEPSIS | | | |
| subjects affected / exposed | 2 / 225 (0.89%) | 2 / 226 (0.88%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA | | | |
| subjects affected / exposed | 2 / 225 (0.89%) | 4 / 226 (1.77%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| STAPHYLOCOCCAL BACTERAEMIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| POSTOPERATIVE WOUND INFECTION | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 2 / 226 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CYSTITIS | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CELLULITIS | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SEPTIC SHOCK | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| STAPHYLOCOCCAL INFECTION | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTRITIS BACTERIAL | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TOOTH ABSCESS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 225 (0.44%) | 0 / 226 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| WOUND INFECTION | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| METABOLIC ACIDOSIS | | | |
| subjects affected / exposed | 0 / 225 (0.00%) | 1 / 226 (0.44%) | |
| 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 / 225 (0.00%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DIABETES MELLITUS | | | |
| subjects affected / exposed | 1 / 225 (0.44%) | 1 / 226 (0.44%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Placebo + ddAC-PacHP | Atezolizumab +ddAC-PacHP | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 225 / 225 (100.00%) | 226 / 226 (100.00%) | |
| Vascular disorders | | | |
| HOT FLUSH | | | |
| subjects affected / exposed | 25 / 225 (11.11%) | 23 / 226 (10.18%) | |
| occurrences (all) | 28 | 27 | |
| HYPERTENSION | | | |
| subjects affected / exposed | 13 / 225 (5.78%) | 14 / 226 (6.19%) | |
| occurrences (all) | 21 | 23 | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| CHILLS | | | |
| subjects affected / exposed | 13 / 225 (5.78%) | 8 / 226 (3.54%) | |
| occurrences (all) | 14 | 8 | |
| PYREXIA | | | |
| subjects affected / exposed | 42 / 225 (18.67%) | 44 / 226 (19.47%) | |
| occurrences (all) | 66 | 60 | |
| PAIN | | | |
| subjects affected / exposed | 15 / 225 (6.67%) | 15 / 226 (6.64%) | |
| occurrences (all) | 21 | 20 | |
| FATIGUE | | | |
| subjects affected / exposed | 38 / 225 (16.89%) | 61 / 226 (26.99%) | |
| occurrences (all) | 49 | 104 | |
| ASTHENIA | | | |
| subjects affected / exposed | 85 / 225 (37.78%) | 96 / 226 (42.48%) | |
| occurrences (all) | 189 | 197 | |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 29 / 225 (12.89%) | 33 / 226 (14.60%) | |
| occurrences (all) | 43 | 41 | |
| MALAISE | | | |
| subjects affected / exposed | 16 / 225 (7.11%) | 11 / 226 (4.87%) | |
| occurrences (all) | 21 | 20 | |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 16 / 225 (7.11%) | 14 / 226 (6.19%) | |
| occurrences (all) | 17 | 19 | |
| Reproductive system and breast disorders | | | |
| BREAST PAIN | | | |
| subjects affected / exposed | 15 / 225 (6.67%) | 8 / 226 (3.54%) | |
| occurrences (all) | 16 | 8 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| RHINORRHOEA | | | |
| subjects affected / exposed | 13 / 225 (5.78%) | 24 / 226 (10.62%) | |
| occurrences (all) | 17 | 28 | |
| DYSPNOEA | | | |
| subjects affected / exposed | 22 / 225 (9.78%) | 18 / 226 (7.96%) | |
| occurrences (all) | 30 | 21 | |
| EPISTAXIS | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 28 / 225 (12.44%) | 28 / 226 (12.39%) | |
| occurrences (all) | 37 | 30 | |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 13 / 225 (5.78%) | 12 / 226 (5.31%) | |
| occurrences (all) | 14 | 13 | |
| COUGH | | | |
| subjects affected / exposed | 46 / 225 (20.44%) | 37 / 226 (16.37%) | |
| occurrences (all) | 62 | 47 | |
| Psychiatric disorders | | | |
| INSOMNIA | | | |
| subjects affected / exposed | 29 / 225 (12.89%) | 38 / 226 (16.81%) | |
| occurrences (all) | 34 | 46 | |
| ANXIETY | | | |
| subjects affected / exposed | 15 / 225 (6.67%) | 8 / 226 (3.54%) | |
| occurrences (all) | 17 | 8 | |
| Investigations | | | |
| BLOOD LACTATE DEHYDROGENASE INCREASED | | | |
| subjects affected / exposed | 9 / 225 (4.00%) | 12 / 226 (5.31%) | |
| occurrences (all) | 9 | 13 | |
| LYMPHOCYTE COUNT DECREASED | | | |
| subjects affected / exposed | 12 / 225 (5.33%) | 13 / 226 (5.75%) | |
| occurrences (all) | 19 | 21 | |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 12 / 225 (5.33%) | 15 / 226 (6.64%) | |
| occurrences (all) | 16 | 19 | |
| NEUTROPHIL COUNT DECREASED | | | |
| subjects affected / exposed | 29 / 225 (12.89%) | 33 / 226 (14.60%) | |
| occurrences (all) | 47 | 69 | |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 49 / 225 (21.78%) | 65 / 226 (28.76%) | |
| occurrences (all) | 77 | 99 | |
| BLOOD ALKALINE PHOSPHATASE INCREASED | | | |
| subjects affected / exposed | 12 / 225 (5.33%) | 10 / 226 (4.42%) | |
| occurrences (all) | 12 | 12 | |
| EJECTION FRACTION DECREASED | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 19 / 225 (8.44%) | 14 / 226 (6.19%) | |
| occurrences (all) | 25 | 14 | |
| WHITE BLOOD CELL COUNT DECREASED | | | |
| subjects affected / exposed | 10 / 225 (4.44%) | 13 / 226 (5.75%) | |
| occurrences (all) | 16 | 25 | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 63 / 225 (28.00%) | 77 / 226 (34.07%) | |
| occurrences (all) | 93 | 126 | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 14 / 225 (6.22%) | 24 / 226 (10.62%) | |
| occurrences (all) | 14 | 25 | |
| Injury, poisoning and procedural complications | | | |
| WOUND COMPLICATION | | | |
| subjects affected / exposed | 16 / 225 (7.11%) | 13 / 226 (5.75%) | |
| occurrences (all) | 16 | 14 | |
| RADIATION SKIN INJURY | | | |
| subjects affected / exposed | 40 / 225 (17.78%) | 51 / 226 (22.57%) | |
| occurrences (all) | 41 | 53 | |
| INFUSION RELATED REACTION | | | |
| subjects affected / exposed | 33 / 225 (14.67%) | 39 / 226 (17.26%) | |
| occurrences (all) | 41 | 58 | |
| PROCEDURAL PAIN | | | |
| subjects affected / exposed | 18 / 225 (8.00%) | 15 / 226 (6.64%) | |
| occurrences (all) | 18 | 15 | |
| Nervous system disorders | | | |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| subjects affected / exposed | 38 / 225 (16.89%) | 46 / 226 (20.35%) | |
| occurrences (all) | 43 | 55 | |
| POLYNEUROPATHY | | | |
| subjects affected / exposed | 13 / 225 (5.78%) | 13 / 226 (5.75%) | |
| occurrences (all) | 15 | 17 | |
| DYSGEUSIA | | | |
| subjects affected / exposed | 35 / 225 (15.56%) | 32 / 226 (14.16%) | |
| occurrences (all) | 40 | 36 | |
| HEADACHE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 48 / 225 (21.33%) | 52 / 226 (23.01%) | |
| occurrences (all) | 67 | 81 | |
| PARAESTHESIA | | | |
| subjects affected / exposed | 20 / 225 (8.89%) | 15 / 226 (6.64%) | |
| occurrences (all) | 24 | 16 | |
| DIZZINESS | | | |
| subjects affected / exposed | 22 / 225 (9.78%) | 23 / 226 (10.18%) | |
| occurrences (all) | 29 | 29 | |
| HYPOAESTHESIA | | | |
| subjects affected / exposed | 9 / 225 (4.00%) | 14 / 226 (6.19%) | |
| occurrences (all) | 11 | 15 | |
| NEUROPATHY PERIPHERAL | | | |
| subjects affected / exposed | 43 / 225 (19.11%) | 43 / 226 (19.03%) | |
| occurrences (all) | 58 | 49 | |
| Blood and lymphatic system disorders | | | |
| LYMPHOPENIA | | | |
| subjects affected / exposed | 13 / 225 (5.78%) | 11 / 226 (4.87%) | |
| occurrences (all) | 28 | 21 | |
| NEUTROPENIA | | | |
| subjects affected / exposed | 76 / 225 (33.78%) | 66 / 226 (29.20%) | |
| occurrences (all) | 188 | 168 | |
| ANAEMIA | | | |
| subjects affected / exposed | 114 / 225 (50.67%) | 114 / 226 (50.44%) | |
| occurrences (all) | 217 | 173 | |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 20 / 225 (8.89%) | 22 / 226 (9.73%) | |
| occurrences (all) | 40 | 31 | |
| LEUKOPENIA | | | |
| subjects affected / exposed | 50 / 225 (22.22%) | 37 / 226 (16.37%) | |
| occurrences (all) | 122 | 105 | |
| Eye disorders | | | |
| DRY EYE | | | |
| subjects affected / exposed | 8 / 225 (3.56%) | 15 / 226 (6.64%) | |
| occurrences (all) | 8 | 15 | |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| GASTROOESOPHAGEAL REFLUX DISEASE | | | |
| subjects affected / exposed | 14 / 225 (6.22%) | 12 / 226 (5.31%) | |
| occurrences (all) | 16 | 19 | |
| CONSTIPATION | | | |
| subjects affected / exposed | 59 / 225 (26.22%) | 67 / 226 (29.65%) | |
| occurrences (all) | 78 | 92 | |
| VOMITING | | | |
| subjects affected / exposed | 53 / 225 (23.56%) | 77 / 226 (34.07%) | |
| occurrences (all) | 86 | 116 | |
| DRY MOUTH | | | |
| subjects affected / exposed | 14 / 225 (6.22%) | 13 / 226 (5.75%) | |
| occurrences (all) | 15 | 13 | |
| DIARRHOEA | | | |
| subjects affected / exposed | 137 / 225 (60.89%) | 145 / 226 (64.16%) | |
| occurrences (all) | 271 | 333 | |
| NAUSEA | | | |
| subjects affected / exposed | 138 / 225 (61.33%) | 145 / 226 (64.16%) | |
| occurrences (all) | 281 | 313 | |
| STOMATITIS | | | |
| subjects affected / exposed | 44 / 225 (19.56%) | 49 / 226 (21.68%) | |
| occurrences (all) | 54 | 66 | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 21 / 225 (9.33%) | 15 / 226 (6.64%) | |
| occurrences (all) | 23 | 16 | |
| DYSPEPSIA | | | |
| subjects affected / exposed | 27 / 225 (12.00%) | 25 / 226 (11.06%) | |
| occurrences (all) | 41 | 27 | |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 29 / 225 (12.89%) | 25 / 226 (11.06%) | |
| occurrences (all) | 36 | 29 | |
| HAEMORRHOIDS | | | |
| subjects affected / exposed | 14 / 225 (6.22%) | 16 / 226 (7.08%) | |
| occurrences (all) | 15 | 16 | |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|---|---|---|---|
| RASH | | | |
| subjects affected / exposed | 46 / 225 (20.44%) | 65 / 226 (28.76%) | |
| occurrences (all) | 58 | 96 | |
| ONYCHOLYSIS | | | |
| subjects affected / exposed | 6 / 225 (2.67%) | 13 / 226 (5.75%) | |
| occurrences (all) | 9 | 15 | |
| DERMATITIS | | | |
| subjects affected / exposed | 13 / 225 (5.78%) | 20 / 226 (8.85%) | |
| occurrences (all) | 14 | 22 | |
| PRURITUS | | | |
| subjects affected / exposed | 23 / 225 (10.22%) | 33 / 226 (14.60%) | |
| occurrences (all) | 33 | 38 | |
| ERYTHEMA | | | |
| subjects affected / exposed | 17 / 225 (7.56%) | 12 / 226 (5.31%) | |
| occurrences (all) | 23 | 19 | |
| NAIL DISORDER | | | |
| subjects affected / exposed | 21 / 225 (9.33%) | 17 / 226 (7.52%) | |
| occurrences (all) | 21 | 19 | |
| ALOPECIA | | | |
| subjects affected / exposed | 141 / 225 (62.67%) | 145 / 226 (64.16%) | |
| occurrences (all) | 150 | 149 | |
| DRY SKIN | | | |
| subjects affected / exposed | 20 / 225 (8.89%) | 21 / 226 (9.29%) | |
| occurrences (all) | 21 | 23 | |
| NAIL DISCOLOURATION | | | |
| subjects affected / exposed | 24 / 225 (10.67%) | 17 / 226 (7.52%) | |
| occurrences (all) | 24 | 17 | |
| Renal and urinary disorders | | | |
| DYSURIA | | | |
| subjects affected / exposed | 16 / 225 (7.11%) | 19 / 226 (8.41%) | |
| occurrences (all) | 20 | 23 | |
| Endocrine disorders | | | |
| HYPERTHYROIDISM | | | |
| subjects affected / exposed | 6 / 225 (2.67%) | 22 / 226 (9.73%) | |
| occurrences (all) | 7 | 25 | |
| HYPOTHYROIDISM | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 21 / 225 (9.33%) | 48 / 226 (21.24%) | |
| occurrences (all) | 23 | 59 | |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 18 / 225 (8.00%) | 22 / 226 (9.73%) | |
| occurrences (all) | 20 | 27 | |
| BONE PAIN | | | |
| subjects affected / exposed | 16 / 225 (7.11%) | 14 / 226 (6.19%) | |
| occurrences (all) | 19 | 15 | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 51 / 225 (22.67%) | 51 / 226 (22.57%) | |
| occurrences (all) | 78 | 75 | |
| MYALGIA | | | |
| subjects affected / exposed | 41 / 225 (18.22%) | 45 / 226 (19.91%) | |
| occurrences (all) | 65 | 61 | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 23 / 225 (10.22%) | 25 / 226 (11.06%) | |
| occurrences (all) | 31 | 38 | |
| Infections and infestations | | | |
| NASOPHARYNGITIS | | | |
| subjects affected / exposed | 15 / 225 (6.67%) | 17 / 226 (7.52%) | |
| occurrences (all) | 17 | 20 | |
| CONJUNCTIVITIS | | | |
| subjects affected / exposed | 17 / 225 (7.56%) | 14 / 226 (6.19%) | |
| occurrences (all) | 17 | 16 | |
| PARONYCHIA | | | |
| subjects affected / exposed | 13 / 225 (5.78%) | 13 / 226 (5.75%) | |
| occurrences (all) | 16 | 13 | |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 19 / 225 (8.44%) | 19 / 226 (8.41%) | |
| occurrences (all) | 20 | 23 | |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 24 / 225 (10.67%) | 23 / 226 (10.18%) | |
| occurrences (all) | 29 | 33 | |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---|---|---|
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 4 / 225 (1.78%) | 13 / 226 (5.75%) | |
| occurrences (all) | 5 | 15 | |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 10 / 225 (4.44%) | 12 / 226 (5.31%) | |
| occurrences (all) | 12 | 15 | |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 14 / 225 (6.22%) | 12 / 226 (5.31%) | |
| occurrences (all) | 22 | 20 | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 34 / 225 (15.11%) | 45 / 226 (19.91%) | |
| occurrences (all) | 43 | 61 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 22 March 2019 | The following updates were made: [1] Trastuzumab emtansine was added as a therapeutic optional therapy in combination with atezolizumab/placebo in the adjuvant setting for participants who did not achieve pathological complete response (pCR); [2] Secondary efficacy endpoints were added; [3] Tissue requirements at screening were clarified; [4] Participants with synchronous bilateral invasive breast cancer, ulcerating and inflammatory breast cancer were excluded; [5] Trastuzumab emtansine, doxorubicin, cyclophosphamide, and paclitaxel were included as investigational medicinal products; [6] Screening mammograms were performed prior to the start of the study; [7] Updated information regarding<br>immune-related nephritis and immune-related myositis risks associated with the administration of atezolizumab; [8] Reference to the continuation and discontinuation of study treatment on the basis of left ventricular ejection fraction (LVEF) measurements. |
| 04 June 2019 | The following updates were made: [1] To provide statistical power to test the primary endpoint of pathological complete response (pCR); [2] An extended China enrollment was added; [3] Participant population and the study rationale was updated; [4] Clarifications were added in regards to the full axillary lymph node dissection; [5] The approved dosage and administration for atezolizumab was added; [6] Clarification of the requirements for performing breast imaging and the performance and intent of tumor assessments; [7] The prescribing information was specified; [8] There was an increase in sites and sample size; [9] Revisions were made to align with the Atezolizumab Investigator's Brochure. |
| 14 February 2020 | The following updates were made: [1] Protocol aligns with atezolizumab Investigator’s Brochure, Version 15; [2] Updates to management guidelines for infusion-related reactions; [3] “Immune-related” was changed to “immune-mediated;” [4] The atezolizumab AE management guidelines for immune mediated myocarditis was revised; [5] The list of potential risks for atezolizumab was revised; [6] Exclusion criteria was updated; [7] Investigational therapy was no longer prohibited during the duration of the study; [8] Clarification that data on breast cancer surgery and pathological assessment was collected from participants who discontinued study treatment during the neoadjuvant phase; [9] Certain participants in the adjuvant phase were not required to provide PK and ADA samples; [10] Participants who discontinued treatment with trastuzumab emtansine for pneumonitis had to discontinue all study treatment. |
| 12 February 2021 | The following updates were made: [1] The independent Data Monitoring Committee (iDMC) recommended to stop treatment with atezolizumab/placebo; [2] China extension phase was cancelled; [3] PK and ADA samples for atezolizumab, trastuzumab and pertuzumab was discontinued during the study treatment phase; [4] Participants would enter the follow-up phase and undergo follow up assessments regardless of reason for discontinuing; [5] Extension of the LVEF assessments; [6] Clarification of continuation of HER2-targeted therapy following Medical Monitor approval; [7] Updates to appendices 9 and 12; [8] Alignment with Investigator's Brochure v17. |

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.

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| On February 5, 2021, the experimental treatment was discontinued and unblinded following the recommendation of the independent Data Monitoring Committee (iDMC) to stop treatment with atezolizumab/placebo. |

Notes: