



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	24 August 2023

Results information

Result version number	v4 (current)
This version publication date	27 October 2024
First version publication date	06 February 2022
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Updates based on NIH comments

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	Final
Date of interim/final analysis	24 August 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	24 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study (also known as IMpassion050) was 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/m² on Day 2 of a 14 day cycle for cycles 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/m² on Day 2 of a 14 day cycle for cycles 1-4.

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.

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	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/m² for 12 continuous weeks (cycles 5-8).

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	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/m² on Day 2 of a 14 day cycle for cycles 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/m² on Day 2 of a 14 day cycle for cycles 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/m² 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	206	205
Not completed	20	23
Consent withdrawn by subject	5	6
Physician decision	-	2
Death	11	13
TSH result is unstable	-	1
Disease relapse	1	-
Lost to follow-up	3	-
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			
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			
Units: years			
arithmetic mean	50.3	50.8	-
standard deviation	± 10.7	± 10.4	-
Sex: Female, Male			
Units: Participants			
Male	1	1	2
Female	225	227	452

Race			
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			
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/m ² & cyclophosphamide 600 mg/m ² IV), followed by atezo 1200 mg IV Q3W for 4 cycles with paclitaxel 80 mg/m ² 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/m ² & cyclophosphamide 600 mg/m ² IV), followed by placebo 1200 mg IV Q3W for 4 cycles with paclitaxel 80 mg/m ² 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 Participants				
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. 9999999 = The median time to event based on Kaplan-Meier estimates was not reached.	
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	226	228		
Units: Months				
median (confidence interval 95%)				
All Participants (n=226,228)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
PD-L1 IC1/2/3 Participants (n=109,109)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
PD-L1 IC0 Participants (n=117,119)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
ER/PgR Negative Participants (n=110,110)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
ER/PgR Positive Participants (n=116,117)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		

Statistical analyses

Statistical analysis title	All Participants
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.59

Statistical analysis title	ER/PgR Positive Participants
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	1.36

Statistical analysis title	ER/PgR Negative Participants
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.28

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	2.82

Statistical analysis title	PD-L1 IC1/2/3
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	4.32

Statistical analysis title	PD-L1 IC0 Participants
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	1.22

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 DFS-evaluable population is defined as participants in the ITT population who undergo surgery. 9999999 = The median time to event based on Kaplan-Meier estimates was not reached.	
End point type	Secondary

End point timeframe:

Time from surgery to first documented disease recurrence or death from any cause (up to

End point values	Atezolizumab +ddAC-PacHP	Placebo + ddAC-PacHP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	217		
Units: Months				
median (confidence interval 95%)				
All Participants (n=217,217)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
PD-L1 IC1/2/3 (n=104,106)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
PD-L1 IC0 (n=113,113)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		

Statistical analyses

Statistical analysis title	All Participants
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	434
Analysis specification	Pre-specified
Analysis type	
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	1.32

Statistical analysis title	PD-L1 IC0
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	434
Analysis specification	Pre-specified
Analysis type	
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.44

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	1.02

Statistical analysis title	PD-L1 IC1/2/3
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	434
Analysis specification	Pre-specified
Analysis type	
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	3.69

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. 9999999 = The median time to event based on Kaplan-Meier estimates was not reached.	
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	226	228		
Units: Months				
median (confidence interval 95%)				
All Participants (n=226,228)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
PD-L1 IC1/2/3 (n=109,109)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
PD-L1 IC0 (n=117,119)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		

Statistical analyses

Statistical analysis title	All Participants
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	2

Statistical analysis title	PD-L1 IC1/2/3
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	7.33

Statistical analysis title	PD-L1 IC0
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.58

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	1.59

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 end of study (approximately 4 years and 7 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 ^[3]
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:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical 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 ^[4]
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:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical 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 (\pm 114)			
-----------------------	------------------	--	--	--

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Concentration (C_{trough}) for Pertuzumab and Trastuzumab in Serum

End point title	Trough Concentration (C _{trough}) 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 (\pm 40.7)	94.8 (\pm 39.8)		
Pertuzumab: C12D1/predose (n=150, 147)	87.7 (\pm 58.4)	91.6 (\pm 59.7)		
Trastuzumab: C8D1/predose (n=205, 201)	58.5 (\pm 29.1)	56.5 (\pm 23.9)		
Trastuzumab: C12D1/predose (n=150, 147)	62.4 (\pm 32.7)	60.4 (\pm 30.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: C_{max} of Trastuzumab Emtansine in Serum

End point title	C _{max} of Trastuzumab Emtansine in Serum
-----------------	--

End point description:

C_{max} 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.

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

End point timeframe:

Day 1 of Cycle 9 and Cycle 12, at treatment discontinuation 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	53	49		
Units: ug/mL				
arithmetic mean (standard deviation)				
C9D1 (n=52,46)	84.3 (± 29.0)	80.5 (± 26.8)		
C12D1 (n=49,46)	82.0 (± 32.2)	82.0 (± 37.2)		

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.	
End point type	Secondary
End point timeframe:	
Day 1 of Cycle 9 and Cycle 12, at treatment discontinuation 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	53	49		
Units: ug/mL				
arithmetic mean (standard deviation)				
C9D1	2.18 (± 5.09)	1.22 (± 1.49)		

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 ^[5]
-----------------	---

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 evaluable 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:

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

Justification: No statistical 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 (n=225)	1			
BL: ADA Negative (n=225)	224			
Post-BL: Treatment-Emergent ADA Positive (n=225)	7			
Post-BL: Treatment-Emergent ADA Negative (n=225)	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 evaluable 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	226	225		
Units: Participants				
number (not applicable)				
BL: ADA Positive (n=216, 207)	2	1		
BL: ADA Negative (216, 207)	214	206		
Post-BL: Trt.-Emergent ADA Positive (n=213, 216)	1	0		
Post-BL: Trt.-Emergent ADA Negative (n=212, 216)	212	216		

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 evaluable 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	226	225		
Units: Participants				
number (not applicable)				
BL: ADA Positive (n=216, 209)	6	3		

BL: ADA Negative (n=216, 209)	210	206		
Post-BL: Trt-Emergent ADA Positive (n=213, 217)	4	3		
Post-BL: Trt-Emergent ADA Negative (n=213, 217)	209	214		

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 (TE) 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).

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

End point timeframe:

Day 1 of Cycle 9 and Cycle 12, at treatment discontinuation 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	57	55		
Units: Participants				
number (not applicable)				
BL: ADA Positive (n=52,50)	3	2		
BL: ADA Negative (n=52, 50)	49	48		
Post-BL: TE ADA Positive (n=57,55)	1	1		
Post-BL: TE ADA Negative (n=57,55)	56	54		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with pCR Based on PIK3CA Mutation Status

End point title	Percentage of Participants 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=40, 34)	59.7	55.7		
Wildtype (n=98, 101)	65.3	65.2		
Missing (n=3, 8)	33.3	66.7		

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:

9999999 = Too few events to calculate the median and 95% confidence intervals.

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	226	228		
Units: Months				
median (confidence interval 95%)				
Missing (n=9,12)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
Mutated (n=67,61)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		

Wildtype (n=150,155)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
----------------------	------------------------------------	------------------------------------	--	--

Statistical analyses

Statistical analysis title	PIK3CA-Missing
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	superiority ^[6]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	2.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	26.42

Notes:

[6] - The overall number of participants analyzed is 21 (n=9,12)

Statistical analysis title	PIK3CA-Wildtype
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	superiority ^[7]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	1.87

Notes:

[7] - The overall number of participants analyzed is 305 (n=150,155)

Statistical analysis title	PIK3CA-Mutated
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	superiority ^[8]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	1.9

Notes:

[8] - The overall number of participants analyzed is 128 (n=67,61)

Secondary: DFS Based on PIK3CA Mutation Status

End point title	DFS Based on PIK3CA Mutation Status
End point description:	
9999999 = Too few events to calculate the median and 95% confidence intervals.	
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	217	217		
Units: Months				
median (confidence interval 95%)				
Missing (n=8,11)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
Mutated (n=66,57)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
Wildtype (n=143,149)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		

Statistical analyses

Statistical analysis title	PIK3CA-Missing
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	434
Analysis specification	Pre-specified
Analysis type	superiority ^[9]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	18.91

Notes:

[9] - The overall number of participants analyzed is 19 (n=8,11)

Statistical analysis title	PIK3CA-Wildtype
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	434
Analysis specification	Pre-specified
Analysis type	superiority ^[10]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	1.55

Notes:

[10] - The overall number of participants analyzed is 292 (n=143,149)

Statistical analysis title	PIK3CA-Mutated
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	434
Analysis specification	Pre-specified
Analysis type	superiority ^[11]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	1.92

Notes:

[11] - The overall number of participants analyzed is 123 (n=66,57)

Secondary: OS Based on PIK3CA Mutation Status

End point title	OS Based on PIK3CA Mutation Status
End point description:	9999999 = Too few events to calculate the median and 95% confidence intervals.
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	226	228		
Units: Months				
median (confidence interval 95%)				
Missing (n=9,12)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
Mutated (n=67,61)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		
Wildtype (n=150,155)	9999999 (9999999 to 9999999)	9999999 (9999999 to 9999999)		

Statistical analyses

Statistical analysis title	PIK3CA-Missing ^[12]
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	superiority ^[13]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	999.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0

Notes:

[12] - A low or upper value for the confidence interval may be missing. Values for both the lower and upper limit are expected to be provided with a 2-sided confidence interval.

Justification: There is no upper limit to report.

[13] - The overall number of participants analyzed is 21 (n=9,12)

The point estimate is >999.99

Statistical analysis title	PIK3CA-Wildtype
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	superiority ^[14]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	2.09

Notes:

[14] - The overall number of participants analyzed is 305 (n=150,155)

Statistical analysis title	PIK3CA-Mutated
Comparison groups	Atezolizumab +ddAC-PacHP v Placebo + ddAC-PacHP
Number of subjects included in analysis	454
Analysis specification	Pre-specified
Analysis type	superiority ^[15]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	3.53

Notes:

[15] - The overall number of participants analyzed is 128 (n=67,61)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From randomization up until end of study (approximately 4 years and 7 months)

Adverse event reporting additional description:

All-cause mortality was reported based on the Intention-to-Treat (ITT) Population = all randomized participants.

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	26.0
--------------------	------

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.

Serious adverse events	Atezolizumab +ddAC-PacHP	Placebo + ddAC-PacHP	
Total subjects affected by serious adverse events			
subjects affected / exposed	65 / 226 (28.76%)	47 / 225 (20.89%)	
number of deaths (all causes)	11	13	
number of deaths resulting from adverse events	2	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Nervous system neoplasm benign			

subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Thrombosis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pain			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian vein thrombosis			
subjects affected / exposed	2 / 226 (0.88%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jugular vein thrombosis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fatigue			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (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	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	3 / 226 (1.33%)	3 / 225 (1.33%)	
occurrences causally related to treatment / all	0 / 3	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Sarcoidosis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Adnexal torsion			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated lung disease			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	1 / 226 (0.44%)	3 / 225 (1.33%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	10 / 226 (4.42%)	2 / 225 (0.89%)	
occurrences causally related to treatment / all	9 / 10	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alveolitis			
subjects affected / exposed	1 / 226 (0.44%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			

subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (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	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Lipase increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	0 / 226 (0.00%)	2 / 225 (0.89%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (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	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glycosylated haemoglobin increased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Platelet count decreased			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (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	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Radiation pneumonitis			
subjects affected / exposed	1 / 226 (0.44%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound complication			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Implantation complication			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Cardiac failure acute			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (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	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	3 / 226 (1.33%)	5 / 225 (2.22%)	
occurrences causally related to treatment / all	3 / 3	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restrictive cardiomyopathy			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			

subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis noninfective			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aplastic anaemia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			

subjects affected / exposed	1 / 226 (0.44%)	1 / 225 (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	10 / 226 (4.42%)	3 / 225 (1.33%)	
occurrences causally related to treatment / all	11 / 12	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 226 (0.44%)	2 / 225 (0.89%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Meibomianitis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye discharge			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated pancreatitis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			

subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (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 / 226 (0.44%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 226 (0.44%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hypertransaminaemia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic haemorrhage			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Steatohepatitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (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	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	2 / 226 (0.88%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypophysitis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Secondary adrenocortical insufficiency			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal insufficiency			
subjects affected / exposed	4 / 226 (1.77%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastritis bacterial			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 226 (0.88%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (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	4 / 226 (1.77%)	2 / 225 (0.89%)	
occurrences causally related to treatment / all	1 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval cellulitis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (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	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	3 / 226 (1.33%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access site infection			
subjects affected / exposed	0 / 226 (0.00%)	2 / 225 (0.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			

subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastitis			
subjects affected / exposed	3 / 226 (1.33%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	1 / 226 (0.44%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 226 (0.88%)	2 / 225 (0.89%)	
occurrences causally related to treatment / all	0 / 2	2 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			

subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 226 (0.00%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	1 / 226 (0.44%)	1 / 225 (0.44%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	1 / 226 (0.44%)	0 / 225 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Atezolizumab +ddAC-PacHP	Placebo + ddAC-PacHP	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	226 / 226 (100.00%)	225 / 225 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	14 / 226 (6.19%)	13 / 225 (5.78%)	
occurrences (all)	22	21	

Hot flush			
subjects affected / exposed	25 / 226 (11.06%)	25 / 225 (11.11%)	
occurrences (all)	29	28	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	9 / 226 (3.98%)	14 / 225 (6.22%)	
occurrences (all)	9	16	
Asthenia			
subjects affected / exposed	96 / 226 (42.48%)	87 / 225 (38.67%)	
occurrences (all)	193	200	
Pain			
subjects affected / exposed	15 / 226 (6.64%)	17 / 225 (7.56%)	
occurrences (all)	20	23	
Mucosal inflammation			
subjects affected / exposed	32 / 226 (14.16%)	29 / 225 (12.89%)	
occurrences (all)	41	42	
Malaise			
subjects affected / exposed	12 / 226 (5.31%)	16 / 225 (7.11%)	
occurrences (all)	21	21	
Pyrexia			
subjects affected / exposed	44 / 226 (19.47%)	47 / 225 (20.89%)	
occurrences (all)	61	73	
Fatigue			
subjects affected / exposed	63 / 226 (27.88%)	38 / 225 (16.89%)	
occurrences (all)	107	49	
Oedema peripheral			
subjects affected / exposed	15 / 226 (6.64%)	16 / 225 (7.11%)	
occurrences (all)	22	17	
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	11 / 226 (4.87%)	15 / 225 (6.67%)	
occurrences (all)	11	16	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			

subjects affected / exposed	32 / 226 (14.16%)	28 / 225 (12.44%)	
occurrences (all)	35	38	
Dyspnoea			
subjects affected / exposed	19 / 226 (8.41%)	22 / 225 (9.78%)	
occurrences (all)	23	33	
Oropharyngeal pain			
subjects affected / exposed	12 / 226 (5.31%)	13 / 225 (5.78%)	
occurrences (all)	13	14	
Rhinorrhoea			
subjects affected / exposed	25 / 226 (11.06%)	14 / 225 (6.22%)	
occurrences (all)	29	18	
Cough			
subjects affected / exposed	39 / 226 (17.26%)	48 / 225 (21.33%)	
occurrences (all)	50	65	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	39 / 226 (17.26%)	29 / 225 (12.89%)	
occurrences (all)	48	36	
Anxiety			
subjects affected / exposed	9 / 226 (3.98%)	14 / 225 (6.22%)	
occurrences (all)	9	16	
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	12 / 226 (5.31%)	10 / 225 (4.44%)	
occurrences (all)	13	10	
Lymphocyte count decreased			
subjects affected / exposed	13 / 226 (5.75%)	12 / 225 (5.33%)	
occurrences (all)	21	20	
Neutrophil count decreased			
subjects affected / exposed	33 / 226 (14.60%)	29 / 225 (12.89%)	
occurrences (all)	69	47	
Weight decreased			
subjects affected / exposed	26 / 226 (11.50%)	17 / 225 (7.56%)	
occurrences (all)	27	17	
Ejection fraction decreased			

subjects affected / exposed	17 / 226 (7.52%)	19 / 225 (8.44%)	
occurrences (all)	17	26	
Blood alkaline phosphatase increased			
subjects affected / exposed	11 / 226 (4.87%)	14 / 225 (6.22%)	
occurrences (all)	14	16	
Platelet count decreased			
subjects affected / exposed	17 / 226 (7.52%)	13 / 225 (5.78%)	
occurrences (all)	23	19	
Aspartate aminotransferase increased			
subjects affected / exposed	69 / 226 (30.53%)	51 / 225 (22.67%)	
occurrences (all)	105	78	
White blood cell count decreased			
subjects affected / exposed	13 / 226 (5.75%)	10 / 225 (4.44%)	
occurrences (all)	25	16	
Alanine aminotransferase increased			
subjects affected / exposed	82 / 226 (36.28%)	65 / 225 (28.89%)	
occurrences (all)	138	98	
Injury, poisoning and procedural complications			
Radiation skin injury			
subjects affected / exposed	52 / 226 (23.01%)	42 / 225 (18.67%)	
occurrences (all)	54	43	
Wound complication			
subjects affected / exposed	13 / 226 (5.75%)	16 / 225 (7.11%)	
occurrences (all)	14	16	
Procedural pain			
subjects affected / exposed	14 / 226 (6.19%)	18 / 225 (8.00%)	
occurrences (all)	14	19	
Infusion related reaction			
subjects affected / exposed	39 / 226 (17.26%)	33 / 225 (14.67%)	
occurrences (all)	57	42	
Nervous system disorders			
Polyneuropathy			
subjects affected / exposed	14 / 226 (6.19%)	13 / 225 (5.78%)	
occurrences (all)	19	15	
Peripheral sensory neuropathy			

subjects affected / exposed	47 / 226 (20.80%)	40 / 225 (17.78%)	
occurrences (all)	56	45	
Hypoaesthesia			
subjects affected / exposed	14 / 226 (6.19%)	9 / 225 (4.00%)	
occurrences (all)	17	11	
Neuropathy peripheral			
subjects affected / exposed	43 / 226 (19.03%)	45 / 225 (20.00%)	
occurrences (all)	50	59	
Paraesthesia			
subjects affected / exposed	15 / 226 (6.64%)	20 / 225 (8.89%)	
occurrences (all)	16	25	
Dysgeusia			
subjects affected / exposed	33 / 226 (14.60%)	35 / 225 (15.56%)	
occurrences (all)	37	40	
Dizziness			
subjects affected / exposed	23 / 226 (10.18%)	23 / 225 (10.22%)	
occurrences (all)	30	30	
Headache			
subjects affected / exposed	53 / 226 (23.45%)	50 / 225 (22.22%)	
occurrences (all)	82	69	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	22 / 226 (9.73%)	22 / 225 (9.78%)	
occurrences (all)	31	45	
Anaemia			
subjects affected / exposed	116 / 226 (51.33%)	118 / 225 (52.44%)	
occurrences (all)	179	235	
Leukopenia			
subjects affected / exposed	37 / 226 (16.37%)	50 / 225 (22.22%)	
occurrences (all)	104	130	
Lymphopenia			
subjects affected / exposed	11 / 226 (4.87%)	13 / 225 (5.78%)	
occurrences (all)	21	28	
Neutropenia			
subjects affected / exposed	66 / 226 (29.20%)	76 / 225 (33.78%)	
occurrences (all)	173	197	

Eye disorders			
Dry eye			
subjects affected / exposed	15 / 226 (6.64%)	9 / 225 (4.00%)	
occurrences (all)	15	9	
Gastrointestinal disorders			
Stomatitis			
subjects affected / exposed	51 / 226 (22.57%)	46 / 225 (20.44%)	
occurrences (all)	68	56	
Dyspepsia			
subjects affected / exposed	27 / 226 (11.95%)	27 / 225 (12.00%)	
occurrences (all)	29	42	
Vomiting			
subjects affected / exposed	78 / 226 (34.51%)	53 / 225 (23.56%)	
occurrences (all)	115	89	
Abdominal pain upper			
subjects affected / exposed	25 / 226 (11.06%)	29 / 225 (12.89%)	
occurrences (all)	28	36	
Dry mouth			
subjects affected / exposed	13 / 226 (5.75%)	14 / 225 (6.22%)	
occurrences (all)	13	15	
Abdominal pain			
subjects affected / exposed	16 / 226 (7.08%)	22 / 225 (9.78%)	
occurrences (all)	17	24	
Haemorrhoids			
subjects affected / exposed	16 / 226 (7.08%)	14 / 225 (6.22%)	
occurrences (all)	16	15	
Diarrhoea			
subjects affected / exposed	146 / 226 (64.60%)	139 / 225 (61.78%)	
occurrences (all)	335	278	
Nausea			
subjects affected / exposed	145 / 226 (64.16%)	139 / 225 (61.78%)	
occurrences (all)	323	287	
Constipation			
subjects affected / exposed	70 / 226 (30.97%)	61 / 225 (27.11%)	
occurrences (all)	95	80	
Gastrooesophageal reflux disease			

subjects affected / exposed occurrences (all)	12 / 226 (5.31%) 19	14 / 225 (6.22%) 17	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	63 / 226 (27.88%)	49 / 225 (21.78%)	
occurrences (all)	96	62	
Alopecia			
subjects affected / exposed	151 / 226 (66.81%)	146 / 225 (64.89%)	
occurrences (all)	158	156	
Dry skin			
subjects affected / exposed	23 / 226 (10.18%)	21 / 225 (9.33%)	
occurrences (all)	25	22	
Onycholysis			
subjects affected / exposed	14 / 226 (6.19%)	6 / 225 (2.67%)	
occurrences (all)	16	9	
Pruritus			
subjects affected / exposed	36 / 226 (15.93%)	25 / 225 (11.11%)	
occurrences (all)	42	35	
Erythema			
subjects affected / exposed	14 / 226 (6.19%)	17 / 225 (7.56%)	
occurrences (all)	20	21	
Dermatitis			
subjects affected / exposed	22 / 226 (9.73%)	13 / 225 (5.78%)	
occurrences (all)	24	14	
Nail discolouration			
subjects affected / exposed	17 / 226 (7.52%)	25 / 225 (11.11%)	
occurrences (all)	17	25	
Nail disorder			
subjects affected / exposed	18 / 226 (7.96%)	22 / 225 (9.78%)	
occurrences (all)	20	23	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	19 / 226 (8.41%)	17 / 225 (7.56%)	
occurrences (all)	23	21	
Endocrine disorders			

Hyperthyroidism subjects affected / exposed occurrences (all)	23 / 226 (10.18%) 27	7 / 225 (3.11%) 8	
Hypothyroidism subjects affected / exposed occurrences (all)	48 / 226 (21.24%) 58	20 / 225 (8.89%) 22	
Musculoskeletal and connective tissue disorders			
Myalgia subjects affected / exposed occurrences (all)	45 / 226 (19.91%) 61	42 / 225 (18.67%) 66	
Bone pain subjects affected / exposed occurrences (all)	15 / 226 (6.64%) 16	19 / 225 (8.44%) 22	
Arthralgia subjects affected / exposed occurrences (all)	59 / 226 (26.11%) 88	52 / 225 (23.11%) 79	
Pain in extremity subjects affected / exposed occurrences (all)	27 / 226 (11.95%) 42	23 / 225 (10.22%) 31	
Back pain subjects affected / exposed occurrences (all)	23 / 226 (10.18%) 29	19 / 225 (8.44%) 21	
Infections and infestations			
COVID-19 subjects affected / exposed occurrences (all)	8 / 226 (3.54%) 8	14 / 225 (6.22%) 14	
Paronychia subjects affected / exposed occurrences (all)	14 / 226 (6.19%) 14	13 / 225 (5.78%) 16	
Urinary tract infection subjects affected / exposed occurrences (all)	25 / 226 (11.06%) 35	24 / 225 (10.67%) 31	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	20 / 226 (8.85%) 24	21 / 225 (9.33%) 22	
Conjunctivitis			

subjects affected / exposed occurrences (all)	14 / 226 (6.19%) 16	17 / 225 (7.56%) 17	
Nasopharyngitis subjects affected / exposed occurrences (all)	18 / 226 (7.96%) 21	15 / 225 (6.67%) 17	
Metabolism and nutrition disorders			
Hypokalaemia subjects affected / exposed occurrences (all)	12 / 226 (5.31%) 16	10 / 225 (4.44%) 12	
Hypomagnesaemia subjects affected / exposed occurrences (all)	12 / 226 (5.31%) 21	14 / 225 (6.22%) 22	
Hyperglycaemia subjects affected / exposed occurrences (all)	14 / 226 (6.19%) 16	4 / 225 (1.78%) 5	
Decreased appetite subjects affected / exposed occurrences (all)	46 / 226 (20.35%) 62	35 / 225 (15.56%) 43	

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 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.
23 February 2023	The protocol was amended to update safety information and align with the Trastuzumab Emtansine Investigator's Brochure, and Atezolizumab Investigator's Brochure.

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.

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: