



Clinical trial results:

An open-label, two-arm, randomized, single-stage phase II study of ATezolizumab in combination with dual HER2 blockade plus epirubicin as NEoadjuvant therapy for HER2-positive early breast cancer

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2019-002364-27 |
| Trial protocol | AT |
| Global end of trial date | 23 November 2022 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 26 October 2023 |
| First version publication date | 29 September 2023 |
| Version creation reason | • Correction of full data set update of contact |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | ABCSG_52 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Roche ID: ML40391 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | ABCSG (Austrian Breast & Colorectal Cancer Study Group) |
| Sponsor organisation address | Nussdorfer Platz 8/12, Wien, Austria, 1190 |
| Public contact | Trial Office, ABCSG (Austrian Breast & Colorectal Cancer Study Group), +43 14089230, info@abcsbg.at |
| Scientific contact | Dr. Gabriel Rinnerthaler, ABCSG (Austrian Breast & Colorectal Cancer Study Group), +43 14089230, info@abcsbg.at |

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 | 30 May 2022 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 30 May 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 November 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of a neoadjuvant immunochemotherapy regimen consisting of atezolizumab, trastuzumab, pertuzumab and epirubicin in regards to pathologic complete response (pCR = ypT0/is, ypN0) which is assessed in the overall study population at the time of surgery

Protection of trial subjects:

The investigators ensured that patients were given comprehensive oral and written information about the nature, significance, and scope of the study prior to enrolment. The study specific patient information and informed consent form included language to encourage study participants to reach out to the Study Doctor / Study Team in case they had any questions, concerns or doubts. Section 16 specifically referenced a 24/7 contact person to reach out to, the ICF furthermore contained a reference to the local ombudsman / patient advocacy / data privacy officer and the trial sites had the opportunity to hand out Patient Cards to the recruited patients for use in case of emergency which includes the trial site's contact details, information of the study drug(s) and the EudraCT-number. A dedicated DMC was established to ensure patient safety throughout the trial.

Background therapy:

Background therapy of trastuzumab, pertuzumab and epirubicin only in treatment part 2 (in treatment arm A and arm B)

Evidence for comparator:

No

| | |
|---|--------------|
| Actual start date of recruitment | 03 July 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Austria: 58 |
| Worldwide total number of subjects | 58 |
| EEA total number of subjects | 58 |

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 | 0 |

| | |
|---------------------------|----|
| months) | |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 46 |
| From 65 to 84 years | 12 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Recruitment phase for this study was 1.4 years. No follow up was done for this study.

Pre-assignment

Screening details:

A careful check of inclusion and exclusion criteria had to be performed by the Investigators / Site Teams and a centralized web based screening and randomization system was subsequently used which assigned treatment arms electronically, i.e. randomized the participants into the previously described treatment arms.

Period 1

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

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Atezolizumab+Pertuzumab+Trastuzumab+Epirubicin (Arm A) |

Arm description:

For treatment part 1, arm A patients received 2 3-week cycles of pertuzumab (starting with 840 mg iv on cycle 1, followed by 420 mg iv for the subsequent cycle), 2 3-week cycles of trastuzumab (starting with 600 mg sc or 8 mg/kg iv on cycle 1, followed by 600 mg sc or 6 mg/kg iv for the subsequent cycle) and 2 3-week cycles of atezolizumab (1200 mg iv per cycle).

For treatment part 2, arm A patients received 4 3-week cycles of atezolizumab (1200 mg iv per cycle), 4 3-week cycles pertuzumab (420 mg iv per cycle), 4 3-week cycles trastuzumab (600 mg sc or 6 mg/kg iv per cycle) as well as 4 3-week cycles of epirubicin (90 mg/m² per cycle).

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Atezolizumab |
| Investigational medicinal product code | RO5541267/F03 |
| Other name | Tecentriq |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intraventricular use |

Dosage and administration details:

60 mg/ml

| | |
|--|---------------------------------------|
| Investigational medicinal product name | Pertuzumab |
| Investigational medicinal product code | RO4368451 |
| Other name | Perjeta |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

30 mg/ml

| | |
|--|--|
| Investigational medicinal product name | Trastuzumab |
| Investigational medicinal product code | 180288-69-1 |
| Other name | Herceptin |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

120 mg/ml

| | |
|---|--|
| Investigational medicinal product name | Trastuzumab |
| Investigational medicinal product code | 180288-69-1 |
| Other name | Herceptin |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: 150 mg/ml | |
| Arm title | Pertuzumab+Trastuzumab+Epirubicin (Arm B) |

Arm description:

For treatment part 1, arm B patients received 2 3-week cycles of pertuzumab (starting with 840 mg iv on cycle 1, followed by 420 mg iv for the subsequent cycle) and 2 3-week cycles of trastuzumab (starting with 600 mg sc or 8 mg/kg iv on cycle 1, followed by 600 mg sc or 6 mg/kg iv for the subsequent cycle).

For treatment part 2, arm B patients received 4 3-week cycles of atezolizumab (1200 mg iv per cycle), 4 3-week cycles pertuzumab (420 mg iv per cycle), 4 3-week cycles trastuzumab (600 mg sc or 6 mg/kg iv per cycle) as well as 4 3-week cycles of epirubicin (90 mg/m² per cycle).

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pertuzumab |
| Investigational medicinal product code | RO4368451 |
| Other name | Perjeta |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

30 mg/ml

| | |
|--|--|
| Investigational medicinal product name | Trastuzumab |
| Investigational medicinal product code | 180288-69-1 |
| Other name | Herceptin |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

120 mg/ml

| | |
|--|--|
| Investigational medicinal product name | Trastuzumab |
| Investigational medicinal product code | 180288-69-1 |
| Other name | Herceptin |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

150 mg/ml

| Number of subjects in period 1 | Atezolizumab+Pertuzumab+Trastuzumab+Epirubicin (Arm A) | Pertuzumab+Trastuzumab+Epirubicin (Arm B) |
|---------------------------------------|--|---|
| Started | 29 | 29 |
| Completed | 28 | 28 |
| Not completed | 1 | 1 |
| Consent withdrawn by subject | 1 | - |
| Lost to follow-up | - | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Atezolizumab+Pertuzumab+Trastuzumab+Epirubicin (Arm A) |
|-----------------------|--|

Reporting group description:

For treatment part 1, arm A patients received 2 3-week cycles of pertuzumab (starting with 840 mg iv on cycle 1, followed by 420 mg iv for the subsequent cycle), 2 3-week cycles of trastuzumab (starting with 600 mg sc or 8 mg/kg iv on cycle 1, followed by 600 mg sc or 6 mg/kg iv for the subsequent cycle) and 2 3-week cycles of atezolizumab (1200 mg iv per cycle).

For treatment part 2, arm A patients received 4 3-week cycles of atezolizumab (1200 mg iv per cycle), 4 3-week cycles pertuzumab (420 mg iv per cycle), 4 3-week cycles trastuzumab (600 mg sc or 6 mg/kg iv per cycle) as well as 4 3-week cycles of epirubicin (90 mg/m² per cycle).

| | |
|-----------------------|---|
| Reporting group title | Pertuzumab+Trastuzumab+Epirubicin (Arm B) |
|-----------------------|---|

Reporting group description:

For treatment part 1, arm B patients received 2 3-week cycles of pertuzumab (starting with 840 mg iv on cycle 1, followed by 420 mg iv for the subsequent cycle) and 2 3-week cycles of trastuzumab (starting with 600 mg sc or 8 mg/kg iv on cycle 1, followed by 600 mg sc or 6 mg/kg iv for the subsequent cycle).

For treatment part 2, arm B patients received 4 3-week cycles of atezolizumab (1200 mg iv per cycle), 4 3-week cycles pertuzumab (420 mg iv per cycle), 4 3-week cycles trastuzumab (600 mg sc or 6 mg/kg iv per cycle) as well as 4 3-week cycles of epirubicin (90 mg/m² per cycle).

| Reporting group values | Atezolizumab+Pertuzumab+Trastuzumab+Epirubicin (Arm A) | Pertuzumab+Trastuzumab+Epirubicin (Arm B) | Total |
|--|--|---|-------|
| Number of subjects | 29 | 29 | 58 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 24 | 22 | 46 |
| From 65-84 years | 5 | 7 | 12 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Units: years | | | |
| median | 57 | 58 | |
| full range (min-max) | 33 to 77 | 38 to 82 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 29 | 29 | 58 |
| Male | 0 | 0 | 0 |
| Menopausal status | | | |
| Menopausal status at randomization | | | |
| Units: Subjects | | | |
| Premenopausal (incl. perimenopausal) | 15 | 9 | 24 |
| Postmenopausal | 14 | 20 | 34 |

| | | | |
|--|----|----|----|
| TILs | | | |
| Amount of Tumor Infiltrating Lymphocytes (TILs) | | | |
| Units: Subjects | | | |
| <5% | 3 | 3 | 6 |
| >=5% | 26 | 26 | 52 |
| Hormone receptor status | | | |
| Hormone receptor status at randomization | | | |
| Units: Subjects | | | |
| Negative | 8 | 8 | 16 |
| Positive | 21 | 21 | 42 |
| Clinical prognostic stage | | | |
| Units: Subjects | | | |
| <=IIA | 23 | 22 | 45 |
| >=IIB | 6 | 7 | 13 |
| cT-stage | | | |
| Clinical tumor stage | | | |
| Units: Subjects | | | |
| T1c | 9 | 7 | 16 |
| T2 | 16 | 19 | 35 |
| T3 | 4 | 1 | 5 |
| T4b | 0 | 1 | 1 |
| T4c | 0 | 1 | 1 |
| cN-stage | | | |
| Clinical nodal status | | | |
| Units: Subjects | | | |
| N0 | 17 | 18 | 35 |
| N1 | 11 | 10 | 21 |
| N2 | 0 | 1 | 1 |
| N2a | 1 | 0 | 1 |
| Tumor grade | | | |
| Units: Subjects | | | |
| G2 | 12 | 16 | 28 |
| G3 | 17 | 13 | 30 |
| Histological tumor type | | | |
| Units: Subjects | | | |
| Invasive carcinoma of no special type (NST) | 23 | 25 | 48 |
| Invasive lobular carcinoma | 2 | 0 | 2 |
| Mixed invasive NST and lobular carcinoma | 0 | 1 | 1 |
| Other | 4 | 3 | 7 |
| cM-stage | | | |
| Clinical metastasis status | | | |
| Units: Subjects | | | |
| M0 | 29 | 29 | 58 |
| HER2 status | | | |
| Status of human epidermal growth factor receptor 2 | | | |
| Units: Subjects | | | |
| Positive | 29 | 29 | 58 |

| | | | |
|--------------------------|--------------|--------------|---|
| BMI | | | |
| Body Mass Index | | | |
| Units: kg/m ² | | | |
| median | 23.6 | 25.8 | |
| full range (min-max) | 19.5 to 37.8 | 19.1 to 39.4 | - |

Subject analysis sets

| | |
|----------------------------|--------------------|
| Subject analysis set title | ITT |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

The ITT population consists of all patients who were randomized. All cases with missing primary outcome of pathologic complete response (pCR yes/no) are considered as no pCR.

| | | | |
|--|----------|--|--|
| Reporting group values | ITT | | |
| Number of subjects | 58 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |
| Adults (18-64 years) | 46 | | |
| From 65-84 years | 12 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: years | | | |
| median | 57 | | |
| full range (min-max) | 33 to 82 | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 58 | | |
| Male | 0 | | |
| Menopausal status | | | |
| Menopausal status at randomization | | | |
| Units: Subjects | | | |
| Premenopausal (incl. perimenopausal) | 24 | | |
| Postmenopausal | 34 | | |
| TILs | | | |
| Amount of Tumor Infiltrating Lymphocytes (TILs) | | | |
| Units: Subjects | | | |
| <5% | 6 | | |
| ≥5% | 52 | | |
| Hormone receptor status | | | |
| Hormone receptor status at randomization | | | |
| Units: Subjects | | | |
| Negative | 16 | | |

| | | | |
|--|--------------|--|--|
| Positive | 42 | | |
| Clinical prognostic stage | | | |
| Units: Subjects | | | |
| <=IIA | 45 | | |
| >=IIB | 13 | | |
| cT-stage | | | |
| Clinical tumor stage | | | |
| Units: Subjects | | | |
| T1c | 16 | | |
| T2 | 35 | | |
| T3 | 5 | | |
| T4b | 1 | | |
| T4c | 1 | | |
| cN-stage | | | |
| Clinical nodal status | | | |
| Units: Subjects | | | |
| N0 | 35 | | |
| N1 | 21 | | |
| N2 | 1 | | |
| N2a | 1 | | |
| Tumor grade | | | |
| Units: Subjects | | | |
| G2 | 28 | | |
| G3 | 30 | | |
| Histological tumor type | | | |
| Units: Subjects | | | |
| Invasive carcinoma of no special type (NST) | 48 | | |
| Invasive lobular carcinoma | 2 | | |
| Mixed invasive NST and lobular carcinoma | 1 | | |
| Other | 7 | | |
| cM-stage | | | |
| Clinical metastasis status | | | |
| Units: Subjects | | | |
| M0 | 58 | | |
| HER2 status | | | |
| Status of human epidermal growth factor receptor 2 | | | |
| Units: Subjects | | | |
| Positive | 58 | | |
| BMI | | | |
| Body Mass Index | | | |
| Units: kg/m ² | | | |
| median | 24.5 | | |
| full range (min-max) | 19.1 to 39.4 | | |

End points

End points reporting groups

| | |
|-----------------------|--|
| Reporting group title | Atezolizumab+Pertuzumab+Trastuzumab+Epirubicin (Arm A) |
|-----------------------|--|

Reporting group description:

For treatment part 1, arm A patients received 2 3-week cycles of pertuzumab (starting with 840 mg iv on cycle 1, followed by 420 mg iv for the subsequent cycle), 2 3-week cycles of trastuzumab (starting with 600 mg sc or 8 mg/kg iv on cycle 1, followed by 600 mg sc or 6 mg/kg iv for the subsequent cycle) and 2 3-week cycles of atezolizumab (1200 mg iv per cycle).

For treatment part 2, arm A patients received 4 3-week cycles of atezolizumab (1200 mg iv per cycle), 4 3-week cycles pertuzumab (420 mg iv per cycle), 4 3-week cycles trastuzumab (600 mg sc or 6 mg/kg iv per cycle) as well as 4 3-week cycles of epirubicin (90 mg/m² per cycle).

| | |
|-----------------------|---|
| Reporting group title | Pertuzumab+Trastuzumab+Epirubicin (Arm B) |
|-----------------------|---|

Reporting group description:

For treatment part 1, arm B patients received 2 3-week cycles of pertuzumab (starting with 840 mg iv on cycle 1, followed by 420 mg iv for the subsequent cycle) and 2 3-week cycles of trastuzumab (starting with 600 mg sc or 8 mg/kg iv on cycle 1, followed by 600 mg sc or 6 mg/kg iv for the subsequent cycle).

For treatment part 2, arm B patients received 4 3-week cycles of atezolizumab (1200 mg iv per cycle), 4 3-week cycles pertuzumab (420 mg iv per cycle), 4 3-week cycles trastuzumab (600 mg sc or 6 mg/kg iv per cycle) as well as 4 3-week cycles of epirubicin (90 mg/m² per cycle).

| | |
|----------------------------|-----|
| Subject analysis set title | ITT |
|----------------------------|-----|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

The ITT population consists of all patients who were randomized. All cases with missing primary outcome of pathologic complete response (pCR yes/no) are considered as no pCR.

Primary: Pathologic complete response (pCR)

| | |
|-----------------|---|
| End point title | Pathologic complete response (pCR) ^[1] |
|-----------------|---|

End point description:

Proportion (%) of patients with a pathologic complete response (pCR) together with its 95 %Wilson confidence interval in both arms combined and assessed in the ITT study population at the time of surgery is compared to a proportion of 40%

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

End point timeframe:

At surgery

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The treatment arms were not compared against each other but the proportion (%) of patients with a pathologic complete response (pCR) in both arms combined was compared to a predefined proportion of 40%. It was not possible to document this single-arm comparison with a fixed value in the analysis part of the system. The estimated rate with the 95% confidence interval was therefore included in the description.

| End point values | ITT | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 58 ^[2] | | | |
| Units: Subjects | | | | |
| pCR | 35 | | | |
| No PCR | 23 | | | |

Notes:

[2] - The estimated pCR rate is 60.3% with a two-sided 95% confidence interval (CI) of [47.5, 71.9].

Statistical analyses

No statistical analyses for this end point

Secondary: Residual Cancer Burden (RCB)

| | |
|--|------------------------------|
| End point title | Residual Cancer Burden (RCB) |
| End point description: Proportion of patients with Residual Cancer Burden RCB 0/I (RCB index ≤ 1.36) together with its 95 %Wilson confidence interval in both arms combined and assessed in the ITT study population at the time of surgery | |
| End point type | Secondary |
| End point timeframe: At surgery | |

| End point values | ITT | | | |
|-----------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 58 | | | |
| Units: Subjects | | | | |
| RCB 0/I | 44 | | | |
| RCB II/III | 11 | | | |
| Not evaluated | 3 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

| | |
|--|-----------------------------|
| End point title | Overall Response Rate (ORR) |
| End point description: Proportion of patients with overall response defined as radiographic complete or radiographic partial response (rCR or rPR) according to modified Response Evaluation Criteria in Solid Tumors (RECIST) together with its 95 %Wilson confidence interval in both arms combined and assessed in the ITT study population at the time of surgery | |
| End point type | Secondary |
| End point timeframe: At surgery | |

| End point values | ITT | | | |
|--|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 58 | | | |
| Units: Subjects | | | | |
| rCR+rPR (complete or partial response) | 50 | | | |
| rSD (stable disease) | 6 | | | |
| Not evaluated | 2 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

(S)AE reporting was mandatory from the date of informed consent form signature (i.e., screening phase) until 42 days after the last dose of neoadjuvant study treatment.

Adverse event reporting additional description:

Screening Phase: only AEs deemed to be serious (SAEs) and related to protocol mandated and not routinely performed procedures have to be reported.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Atezolizumab+Pertuzumab+Trastuzumab+Epirubicin (Arm A) |
|-----------------------|--|

Reporting group description: -

| | |
|-----------------------|---|
| Reporting group title | Pertuzumab+Trastuzumab+Epirubicin (Arm B) |
|-----------------------|---|

Reporting group description: -

| Serious adverse events | Atezolizumab+Pertuzumab+Trastuzumab+Epirubicin (Arm A) | Pertuzumab+Trastuzumab+Epirubicin (Arm B) | |
|--|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 29 (17.24%) | 6 / 29 (20.69%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | Additional description: Infusion related reaction | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | 3 / 29 (10.34%) | |
| occurrences causally related to treatment / all | 3 / 3 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Cardiomyopathy | Additional description: Cardiomyopathy | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|----------------|--|
| General physical health deterioration | Additional description: General physical health deterioration | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | Additional description: Febrile neutropenia | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Alveolar osteitis | Additional description: Alveolar osteitis | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile infection | Additional description: Febrile infection | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 29 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | Additional description: COVID-19 | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 29 (3.45%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| | | | |
|---|--|---|--|
| Non-serious adverse events | Atezolizumab+Pertuzumab+Trastuzumab+Epirubicin (Arm A) | Pertuzumab+Trastuzumab+Epirubicin (Arm B) | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 29 / 29 (100.00%) | 29 / 29 (100.00%) | |

| | | | |
|--|--|------------------|--|
| Vascular disorders Hot flush alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Hypertension alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Hypotension alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Thrombophlebitis alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | | | |
| | Additional description: Hot flush | | |
| | 3 / 29 (10.34%) | 2 / 29 (6.90%) | |
| | 3 | 2 | |
| | Additional description: Hypertension | | |
| | 2 / 29 (6.90%) | 2 / 29 (6.90%) | |
| | 2 | 2 | |
| | Additional description: Hypotension | | |
| | 2 / 29 (6.90%) | 1 / 29 (3.45%) | |
| | 2 | 1 | |
| | Additional description: Thrombophlebitis | | |
| | 2 / 29 (6.90%) | 0 / 29 (0.00%) | |
| | 2 | 0 | |
| General disorders and administration site conditions Influenza like illness alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Fatigue alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Chills alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Pyrexia alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) Pain | | | |
| | Additional description: Influenza like illness | | |
| | 2 / 29 (6.90%) | 0 / 29 (0.00%) | |
| | 2 | 0 | |
| | Additional description: Fatigue | | |
| | 14 / 29 (48.28%) | 17 / 29 (58.62%) | |
| | 29 | 35 | |
| | Additional description: Chills | | |
| | 7 / 29 (24.14%) | 7 / 29 (24.14%) | |
| | 8 | 7 | |
| | Additional description: Pyrexia | | |
| | 5 / 29 (17.24%) | 7 / 29 (24.14%) | |
| | 8 | 8 | |
| | Additional description: Pain | | |

| | | | |
|---|--|----------------------|--|
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 1 / 29 (3.45%) 1 | |
| Mucosal inflammation | Additional description: Mucosal inflammation | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 5 / 29 (17.24%) 8 | 5 / 29 (17.24%) 6 | |
| Reproductive system and breast disorders | | | |
| Breast pain | Additional description: Breast pain | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 1 / 29 (3.45%) 1 | |
| Vulvovaginal dryness | Additional description: Vulvovaginal dryness | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 0 / 29 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea exertional | Additional description: Dyspnoea exertional | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 2 / 29 (6.90%) 2 | |
| Epistaxis | Additional description: Epistaxis | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 2 / 29 (6.90%) 2 | |
| Rhinorrhoea | Additional description: Rhinorrhoea | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 1 / 29 (3.45%) 1 | |
| Nasal dryness | Additional description: Nasal dryness | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 4 / 29 (13.79%) 4 | |
| Cough | Additional description: Cough | | |

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|---|---|-----------------------|--|
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 4 | 1 / 29 (3.45%) 1 | |
| Psychiatric disorders | | | |
| Sleep disorder | Additional description: Sleep disorder | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 3 | 0 / 29 (0.00%) 0 | |
| Injury, poisoning and procedural complications | | | |
| Infusion related reaction | Additional description: Infusion related reaction | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 3 / 29 (10.34%) 3 | |
| Nervous system disorders | | | |
| Polyneuropathy | Additional description: Polyneuropathy | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 5 | 2 / 29 (6.90%) 2 | |
| Paraesthesia | Additional description: Paraesthesia | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 4 | 2 / 29 (6.90%) 2 | |
| Headache | Additional description: Headache | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 7 / 29 (24.14%) 7 | 8 / 29 (27.59%) 16 | |
| Ageusia | Additional description: Ageusia | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 2 / 29 (6.90%) 2 | |
| Dysgeusia | Additional description: Dysgeusia | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 4 | 1 / 29 (3.45%) 1 | |
| Taste disorder | Additional description: Taste disorder | | |

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|---|---|----------------------|--|
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 3 | 3 / 29 (10.34%) 5 | |
| Blood and lymphatic system disorders | | | |
| Neutropenia | Additional description: Neutropenia | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 6 / 29 (20.69%) 9 | 4 / 29 (13.79%) 7 | |
| Leukopenia | Additional description: Leukopenia | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 3 | 1 / 29 (3.45%) 1 | |
| Anaemia | Additional description: Anaemia | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 6 | 3 / 29 (10.34%) 4 | |
| Ear and labyrinth disorders | | | |
| Vertigo | Additional description: Vertigo | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 10 | 1 / 29 (3.45%) 4 | |
| Eye disorders | | | |
| Dry eye | Additional description: Dry eye | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 3 / 29 (10.34%) 4 | |
| Visual impairment | Additional description: Visual impairment | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 2 / 29 (6.90%) 2 | |
| Gastrointestinal disorders | | | |
| Vomiting | Additional description: Vomiting | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 4 | 2 / 29 (6.90%) 6 | |
| Diarrhoea | Additional description: Diarrhoea | | |

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|---|---|------------------------|--|
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 17 / 29 (58.62%) 42 | 18 / 29 (62.07%) 43 | |
| Nausea | Additional description: Nausea | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 20 / 29 (68.97%) 38 | 20 / 29 (68.97%) 45 | |
| Dyspepsia | Additional description: Dyspepsia | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 5 / 29 (17.24%) 8 | |
| Abdominal pain upper | Additional description: Abdominal pain upper | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 0 / 29 (0.00%) 0 | |
| Abnormal faeces | Additional description: Abnormal faeces | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 2 / 29 (6.90%) 2 | |
| Constipation | Additional description: Constipation | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 5 / 29 (17.24%) 9 | 8 / 29 (27.59%) 15 | |
| Stomatitis | Additional description: Stomatitis | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 3 / 29 (10.34%) 4 | |
| Hepatobiliary disorders | | | |
| Hypertransaminasaemia | Additional description: Hypertransaminasaemia | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 2 | 3 / 29 (10.34%) 3 | |
| Skin and subcutaneous tissue disorders | | | |

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|--|---------------------------------------|-----------------|--|
| Alopecia alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Alopecia | | |
| | 12 / 29 (41.38%) | 8 / 29 (27.59%) | |
| | 14 | 10 | |
| Dry skin alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Dry skin | | |
| | 4 / 29 (13.79%) | 5 / 29 (17.24%) | |
| | 4 | 5 | |
| Eczema alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Eczema | | |
| | 0 / 29 (0.00%) | 3 / 29 (10.34%) | |
| | 0 | 5 | |
| Rash alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Rash | | |
| | 3 / 29 (10.34%) | 4 / 29 (13.79%) | |
| | 3 | 5 | |
| Pruritus alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Pruritus | | |
| | 3 / 29 (10.34%) | 1 / 29 (3.45%) | |
| | 3 | 2 | |
| Nail disorder alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Nail disorder | | |
| | 2 / 29 (6.90%) | 0 / 29 (0.00%) | |
| | 2 | 0 | |
| Intertrigo alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Intertrigo | | |
| | 2 / 29 (6.90%) | 0 / 29 (0.00%) | |
| | 3 | 0 | |
| Renal and urinary disorders | | | |
| Dysuria alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Dysuria | | |
| | 2 / 29 (6.90%) | 0 / 29 (0.00%) | |
| | 2 | 0 | |
| Endocrine disorders | | | |

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|--|---|-----------------|--|
| Immune-mediated hyperthyroidism alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | Additional description: Immune-mediated hyperthyroidism | | |
| | 2 / 29 (6.90%) | 2 / 29 (6.90%) | |
| | 2 | 2 | |
| Musculoskeletal and connective tissue disorders | | | |
| | Additional description: Pain in extremity | | |
| | 1 / 29 (3.45%) | 2 / 29 (6.90%) | |
| | 1 | 3 | |
| | Additional description: Myalgia | | |
| | 3 / 29 (10.34%) | 2 / 29 (6.90%) | |
| | 3 | 3 | |
| | Additional description: Muscle spasms | | |
| | 1 / 29 (3.45%) | 2 / 29 (6.90%) | |
| | 1 | 2 | |
| | Additional description: Back pain | | |
| | 1 / 29 (3.45%) | 3 / 29 (10.34%) | |
| | 3 | 3 | |
| | Additional description: Arthralgia | | |
| | 5 / 29 (17.24%) | 2 / 29 (6.90%) | |
| | 5 | 3 | |
| Infections and infestations | | | |
| | Additional description: Urinary tract infection | | |
| | 4 / 29 (13.79%) | 1 / 29 (3.45%) | |
| | 7 | 2 | |
| | Additional description: Rhinitis | | |
| | 2 / 29 (6.90%) | 2 / 29 (6.90%) | |
| | 2 | 2 | |
| Respiratory tract infection | Additional description: Respiratory tract infection | | |
| | | | |

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|---|--|----------------------|--|
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 2 / 29 (6.90%) 2 | |
| Oral herpes | Additional description: Oral herpes | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 3 | 0 / 29 (0.00%) 0 | |
| Nasopharyngitis | Additional description: Nasopharyngitis | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 5 / 29 (17.24%) 5 | |
| Candida infection | Additional description: Candida infection | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 0 / 29 (0.00%) 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | Additional description: Decreased appetite | | |
| alternative assessment type: Non-systematic subjects affected / exposed occurrences (all) | 6 / 29 (20.69%) 7 | 4 / 29 (13.79%) 6 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported