



Clinical trial results:

A Randomized, Multicenter, Open-Label Cross-Over Study to Evaluate Patient Preference and Satisfaction of Subcutaneous Administration of the Fixed-Dose Combination of Pertuzumab and Trastuzumab in Patients with HER2-Positive Early Breast Cancer

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2018-002153-30 |
| Trial protocol | ES PT SE FI |
| Global end of trial date | 12 October 2022 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v2 |
| This version publication date | 19 October 2023 |
| First version publication date | 04 March 2021 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | MO40628 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03674112 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | F. Hoffmann-La Roche, Ltd. |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070 |
| Public contact | F. Hoffmann-La Roche, Ltd., F. Hoffmann-La Roche, Ltd., +41 616878333, global.trial_information@roche.com |
| Scientific contact | F. Hoffmann-La Roche, Ltd., F. Hoffmann-La Roche, Ltd., +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 | 12 October 2022 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 October 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective for this study is to evaluate patient preference for pertuzumab and trastuzumab FDC SC.

Protection of trial subjects:

This study is conducted in full conformance with the ICH E6 guideline for Good Clinical Practice and the principles of the Declaration of Helsinki, or the laws and regulations of the country in which the research is conducted, whichever affords the greater protection to the individual. All participants are required to read and sign an informed consent form prior to participation in the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 19 December 2018 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Safety |
| Long term follow-up duration | 3 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Argentina: 8 |
| Country: Number of subjects enrolled | Brazil: 10 |
| Country: Number of subjects enrolled | Chile: 8 |
| Country: Number of subjects enrolled | Finland: 10 |
| Country: Number of subjects enrolled | Hong Kong: 8 |
| Country: Number of subjects enrolled | Jordan: 5 |
| Country: Number of subjects enrolled | Lebanon: 3 |
| Country: Number of subjects enrolled | Mexico: 4 |
| Country: Number of subjects enrolled | Panama: 7 |
| Country: Number of subjects enrolled | Portugal: 24 |
| Country: Number of subjects enrolled | Qatar: 2 |
| Country: Number of subjects enrolled | Saudi Arabia: 2 |
| Country: Number of subjects enrolled | Serbia: 22 |
| Country: Number of subjects enrolled | Spain: 18 |
| Country: Number of subjects enrolled | Sweden: 6 |
| Country: Number of subjects enrolled | United States: 23 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 160 |
| 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 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 140 |
| From 65 to 84 years | 20 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 183 patients were screened and 160 participants were enrolled.

Period 1

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

Arms

| | |
|------------------------------|---------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | A: P+H IV Followed by PH FDC SC |

Arm description:

In the Treatment Cross-Over Period of the study, participants randomized to Arm A first received pertuzumab IV and trastuzumab IV (P+H IV) administration for 3 treatment cycles followed by the pertuzumab and trastuzumab fixed-dose combination subcutaneous (PH FDC SC) administration for 3 treatment cycles (1 cycle = 21 days). Following completion of this study period, participants chose one of the two study treatments to receive in the Treatment Continuation Period for the remaining anti-HER2 treatment cycles (18 planned cycles in total, including pre-study neoadjuvant treatment). After completing study treatment, participants entered the Follow-up Period wherein they were to be followed for 3 years from the date the last participant was randomized.

| | |
|--|---------------------------------------|
| 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:

Pertuzumab was non-weight based and was administered as an intravenous (IV) infusion once every 3 weeks (Q3W) in 2 dose configurations as follows: Loading dose of 840 milligrams (mg) IV, and maintenance dose of 420 mg IV. The dose and schedule were consistent with the prescribing information. Loading doses of pertuzumab and trastuzumab (P+H) IV were only required for subjects who had ≥ 6 weeks since their last neoadjuvant dose of P+H at study entry or ≥ 6 weeks since their last study treatment during the study. Maintenance doses were used for subsequent administrations or dose delays < 6 weeks between doses.

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Pertuzumab and trastuzumab FDC SC |
| Investigational medicinal product code | RO7198574 |
| Other name | Phesgo |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

The pertuzumab and trastuzumab fixed-dose combination subcutaneous (FDC SC) administration was non-weight based and was administered as an SC injection to the thigh Q3W in 2 dose configurations as follows: Loading dose of 1200 milligrams (mg) pertuzumab and 600 mg trastuzumab SC; and maintenance dose of 600 mg pertuzumab and 600 mg trastuzumab SC. Loading doses of pertuzumab and trastuzumab (PH) FDC SC were only required for subjects who had ≥ 6 weeks since their last neoadjuvant dose of P+H at study entry or ≥ 6 weeks since their last study treatment during the study. Maintenance doses were used for subsequent administrations or dose delays < 6 weeks between doses.

| | |
|--|-------------|
| Investigational medicinal product name | Trastuzumab |
| Investigational medicinal product code | Ro 45-2317 |
| Other name | Herceptin |

| | |
|--------------------------|--|
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Trastuzumab was weight based and was administered as an intravenous (IV) infusion Q3W after completion of the pertuzumab infusion and observation period in 2 dose configurations as follows: Loading dose of 8 milligrams per kilogram (mg/kg) IV, and maintenance dose of 6 mg/kg IV. The dose and schedule were consistent with the prescribing information. Loading doses of pertuzumab and trastuzumab (P+H) IV were only required for subjects who had ≥ 6 weeks since their last neoadjuvant dose of P+H at study entry or ≥ 6 weeks since their last study treatment during the study. Maintenance doses were used for subsequent administrations or dose delays < 6 weeks between doses.

| | |
|------------------|---------------------------------|
| Arm title | B: PH FDC SC Followed by P+H IV |
|------------------|---------------------------------|

Arm description:

In the Treatment Cross-Over Period of the study, participants randomized to Arm B first received the pertuzumab and trastuzumab fixed-dose combination subcutaneous (PH FDC SC) administration for 3 treatment cycles followed by pertuzumab intravenous (IV) and trastuzumab IV (P+H IV) administration for 3 treatment cycles (1 cycle = 21 days). Following completion of this study period, participants chose one of the two study treatments to receive in the Treatment Continuation Period for the remaining anti-HER2 treatment cycles (18 planned cycles in total, including pre-study neoadjuvant treatment). After completing study treatment, participants entered the Follow-up Period wherein they were to be followed for 3 years from the date the last participant was randomized.

| | |
|--|-----------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Pertuzumab and trastuzumab FDC SC |
| Investigational medicinal product code | RO7198574 |
| Other name | Phesgo |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

The pertuzumab and trastuzumab fixed-dose combination subcutaneous (FDC SC) administration was non-weight based and was administered as an SC injection to the thigh Q3W in 2 dose configurations as follows: Loading dose of 1200 milligrams (mg) pertuzumab and 600 mg trastuzumab SC; and maintenance dose of 600 mg pertuzumab and 600 mg trastuzumab SC. Loading doses of pertuzumab and trastuzumab (PH) FDC SC were only required for subjects who had ≥ 6 weeks since their last neoadjuvant dose of P+H at study entry or ≥ 6 weeks since their last study treatment during the study. Maintenance doses were used for subsequent administrations or dose delays < 6 weeks between doses.

| | |
|--|--|
| Investigational medicinal product name | Trastuzumab |
| Investigational medicinal product code | Ro 45-2317 |
| Other name | Herceptin |
| Pharmaceutical forms | Powder for concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Trastuzumab was weight based and was administered as an intravenous (IV) infusion Q3W after completion of the pertuzumab infusion and observation period in 2 dose configurations as follows: Loading dose of 8 milligrams per kilogram (mg/kg) IV, and maintenance dose of 6 mg/kg IV. The dose and schedule were consistent with the prescribing information. Loading doses of pertuzumab and trastuzumab (P+H) IV were only required for subjects who had ≥ 6 weeks since their last neoadjuvant dose of P+H at study entry or ≥ 6 weeks since their last study treatment during the study. Maintenance doses were used for subsequent administrations or dose delays < 6 weeks between doses.

| | |
|--|---------------------------------------|
| 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:

Pertuzumab was non-weight based and was administered as an intravenous (IV) infusion once every 3 weeks (Q3W) in 2 dose configurations as follows: Loading dose of 840 milligrams (mg) IV, and maintenance dose of 420 mg IV. The dose and schedule were consistent with the prescribing information. Loading doses of pertuzumab and trastuzumab (P+H) IV were only required for subjects who had ≥ 6 weeks since their last neoadjuvant dose of P+H at study entry or ≥ 6 weeks since their last study treatment during the study. Maintenance doses were used for subsequent administrations or dose delays < 6 weeks between doses.

| Number of subjects in period 1 | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV |
|--|--|--|
| Started | 80 | 80 |
| Completed Cross-Over Treatment (C1-6) | 80 | 80 |
| Completed Cross-Over Period | 79 | 80 |
| Started Treatment Continuation | 79 | 80 |
| Completed Continuation Treatment (C7-18) | 78 | 77 |
| Completed Treatment Continuation Period | 78 | 77 |
| Started Follow-Up Period | 80 | 79 |
| Completed Follow-Up Period (≥ 3 Years) | 73 | 75 |
| Completed | 73 | 75 |
| Not completed | 7 | 5 |
| Consent withdrawn by subject | 2 | 3 |
| Death | 2 | - |
| Reason Not Specified | 1 | 1 |
| Lost to follow-up | 2 | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------------------------|
| Reporting group title | A: P+H IV Followed by PH FDC SC |
|-----------------------|---------------------------------|

Reporting group description:

In the Treatment Cross-Over Period of the study, participants randomized to Arm A first received pertuzumab IV and trastuzumab IV (P+H IV) administration for 3 treatment cycles followed by the pertuzumab and trastuzumab fixed-dose combination subcutaneous (PH FDC SC) administration for 3 treatment cycles (1 cycle = 21 days). Following completion of this study period, participants chose one of the two study treatments to receive in the Treatment Continuation Period for the remaining anti-HER2 treatment cycles (18 planned cycles in total, including pre-study neoadjuvant treatment). After completing study treatment, participants entered the Follow-up Period wherein they were to be followed for 3 years from the date the last participant was randomized.

| | |
|-----------------------|---------------------------------|
| Reporting group title | B: PH FDC SC Followed by P+H IV |
|-----------------------|---------------------------------|

Reporting group description:

In the Treatment Cross-Over Period of the study, participants randomized to Arm B first received the pertuzumab and trastuzumab fixed-dose combination subcutaneous (PH FDC SC) administration for 3 treatment cycles followed by pertuzumab intravenous (IV) and trastuzumab IV (P+H IV) administration for 3 treatment cycles (1 cycle = 21 days). Following completion of this study period, participants chose one of the two study treatments to receive in the Treatment Continuation Period for the remaining anti-HER2 treatment cycles (18 planned cycles in total, including pre-study neoadjuvant treatment). After completing study treatment, participants entered the Follow-up Period wherein they were to be followed for 3 years from the date the last participant was randomized.

| Reporting group values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | Total |
|--|---------------------------------|---------------------------------|-------|
| Number of subjects | 80 | 80 | 160 |
| 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) | 68 | 72 | 140 |
| From 65-84 years | 12 | 8 | 20 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 49.4 | 48.2 | - |
| standard deviation | ± 11.6 | ± 12.1 | - |
| Sex: Female, Male Units: Participants | | | |
| Female | 80 | 80 | 160 |
| Male | 0 | 0 | 0 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 17 | 21 | 38 |
| Not Hispanic or Latino | 59 | 54 | 113 |
| Unknown or Not Reported | 4 | 5 | 9 |
| Race (NIH/OMB) | | | |

| | | | |
|--|---------|---------|-----|
| Units: Subjects | | | |
| American Indian or Alaska Native | 5 | 3 | 8 |
| Asian | 8 | 4 | 12 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 2 | 2 | 4 |
| White | 62 | 67 | 129 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 3 | 4 | 7 |
| Eastern Cooperative Oncology Group (ECOG) Performance Status at Baseline | | | |
| ECOG Performance Status: 0 = Fully active, able to carry on all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework or office work. | | | |
| Units: Subjects | | | |
| ECOG Performance Status 0 | 70 | 70 | 140 |
| ECOG Performance Status 1 | 10 | 10 | 20 |
| Number of Cycles of Prior Neoadjuvant Pertuzumab IV and Trastuzumab IV | | | |
| Units: Subjects | | | |
| <4 Cycles | 5 | 10 | 15 |
| ≥4 Cycles | 75 | 70 | 145 |
| Prior Neoadjuvant Chemotherapy Regimen | | | |
| Participants were stratified at randomization according to prior neoadjuvant chemotherapy regimen, pathological complete response to prior neoadjuvant treatment, and hormone receptor status. | | | |
| Units: Subjects | | | |
| Anthracyclines + Taxanes | 55 | 53 | 108 |
| Carboplatin + Taxanes | 22 | 23 | 45 |
| Taxanes Only | 3 | 4 | 7 |
| Pathological Complete Response (pCR) to Prior Neoadjuvant Treatment | | | |
| Participants were stratified at randomization according to prior neoadjuvant chemotherapy regimen, pathological complete response to prior neoadjuvant treatment, and hormone receptor status. | | | |
| Units: Subjects | | | |
| pCR | 52 | 50 | 102 |
| Non-pCR | 28 | 30 | 58 |
| Hormone Receptor Status | | | |
| Participants were stratified at randomization according to prior neoadjuvant chemotherapy regimen, pathological complete response to prior neoadjuvant treatment, and hormone receptor status (estrogen receptor [ER] and progesterone receptor [PgR]). | | | |
| Units: Subjects | | | |
| ER-Positive and/or PgR-Positive | 53 | 51 | 104 |
| ER-Negative and PgR-Negative | 27 | 29 | 56 |
| Baseline Weight | | | |
| Units: kilograms (kg) | | | |
| arithmetic mean | 67.36 | 70.21 | |
| standard deviation | ± 12.08 | ± 14.15 | - |

End points

End points reporting groups

| | |
|-----------------------|---------------------------------|
| Reporting group title | A: P+H IV Followed by PH FDC SC |
|-----------------------|---------------------------------|

Reporting group description:

In the Treatment Cross-Over Period of the study, participants randomized to Arm A first received pertuzumab IV and trastuzumab IV (P+H IV) administration for 3 treatment cycles followed by the pertuzumab and trastuzumab fixed-dose combination subcutaneous (PH FDC SC) administration for 3 treatment cycles (1 cycle = 21 days). Following completion of this study period, participants chose one of the two study treatments to receive in the Treatment Continuation Period for the remaining anti-HER2 treatment cycles (18 planned cycles in total, including pre-study neoadjuvant treatment). After completing study treatment, participants entered the Follow-up Period wherein they were to be followed for 3 years from the date the last participant was randomized.

| | |
|-----------------------|---------------------------------|
| Reporting group title | B: PH FDC SC Followed by P+H IV |
|-----------------------|---------------------------------|

Reporting group description:

In the Treatment Cross-Over Period of the study, participants randomized to Arm B first received the pertuzumab and trastuzumab fixed-dose combination subcutaneous (PH FDC SC) administration for 3 treatment cycles followed by pertuzumab intravenous (IV) and trastuzumab IV (P+H IV) administration for 3 treatment cycles (1 cycle = 21 days). Following completion of this study period, participants chose one of the two study treatments to receive in the Treatment Continuation Period for the remaining anti-HER2 treatment cycles (18 planned cycles in total, including pre-study neoadjuvant treatment). After completing study treatment, participants entered the Follow-up Period wherein they were to be followed for 3 years from the date the last participant was randomized.

| | |
|----------------------------|------------------|
| Subject analysis set title | All Participants |
|----------------------------|------------------|

| | |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

In the Treatment Cross-Over Period of the study, all participants received their first 6 cycles of treatment in accordance with the study arm to which they were randomized: Arm A) pertuzumab IV and trastuzumab IV (P+H IV) for 3 treatment cycles followed by the pertuzumab and trastuzumab fixed-dose combination for subcutaneous administration (PH FDC SC) for 3 treatment cycles (1 cycle = 21 days); or Arm B) PH FDC SC for 3 treatment cycles followed by P+H IV for 3 treatment cycles (1 cycle = 21 days). Following completion of this study period, participants chose one of the two study treatments to receive in the Treatment Continuation Period for the remaining anti-HER2 treatment cycles (18 planned cycles in total, including pre-study neoadjuvant treatment). After completing study treatment, participants entered the Follow-up Period wherein they were to be followed for 3 years from the date the last participant was randomized.

| | |
|----------------------------|--------------------------------------|
| Subject analysis set title | All Participants: TASQ-IV Completers |
|----------------------------|--------------------------------------|

| | |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

This analysis set includes all participants from Arms A and B who completed the TASQ-IV questionnaire, which was administered at the last IV treatment cycle in the Treatment Cross-Over Period of the study. During the Treatment Cross-Over Period, all participants received their first 6 cycles of treatment in accordance with the study arm to which they were randomized: Arm A) pertuzumab IV and trastuzumab IV (P+H IV) for 3 treatment cycles followed by the pertuzumab and trastuzumab fixed-dose combination for subcutaneous administration (PH FDC SC) for 3 treatment cycles (1 cycle = 21 days); or Arm B) PH FDC SC for 3 treatment cycles followed by P+H IV for 3 treatment cycles (1 cycle = 21 days).

| | |
|----------------------------|--------------------------------------|
| Subject analysis set title | All Participants: TASQ-SC Completers |
|----------------------------|--------------------------------------|

| | |
|---------------------------|-----------------------------|
| Subject analysis set type | Modified intention-to-treat |
|---------------------------|-----------------------------|

Subject analysis set description:

This analysis set includes all participants from Arms A and B who completed the TASQ-SC questionnaire, which was administered at the last SC treatment cycle in the Treatment Cross-Over Period of the study. During the Treatment Cross-Over Period, all participants received their first 6 cycles of treatment in accordance with the study arm to which they were randomized: Arm A) pertuzumab IV and trastuzumab IV (P+H IV) for 3 treatment cycles followed by the pertuzumab and trastuzumab fixed-dose combination for subcutaneous administration (PH FDC SC) for 3 treatment cycles (1 cycle = 21 days); or Arm B) PH FDC SC for 3 treatment cycles followed by P+H IV for 3 treatment cycles (1 cycle = 21 days).

| | |
|----------------------------|------------------------------|
| Subject analysis set title | All Healthcare Professionals |
|----------------------------|------------------------------|

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

Subject analysis set description:

This analysis set includes all healthcare professionals who treated participants from Arms A and B and

completed the HCPQ questionnaire, which was administered at the last treatment cycle in the Treatment Cross-Over Period of the study. During the Treatment Cross-Over Period, all participants received their first 6 cycles of treatment in accordance with the study arm to which they were randomized: Arm A) pertuzumab IV and trastuzumab IV (P+H IV) for 3 treatment cycles followed by the pertuzumab and trastuzumab fixed-dose combination for subcutaneous administration (PH FDC SC) for 3 treatment cycles (1 cycle = 21 days); or Arm B) PH FDC SC for 3 treatment cycles followed by P+H IV for 3 treatment cycles (1 cycle = 21 days).

| | |
|----------------------------|---|
| Subject analysis set title | Arm A: Treatment With P+H IV (Cycles 1–3) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

This safety analysis population only includes the adverse events that occurred in Arm A participants during treatment Cycles 1 to 3 when all Arm A participants were treated with P+H IV. In the Treatment Cross-Over Period of the study, participants randomized to Arm A first received treatment with pertuzumab IV and trastuzumab IV (P+H IV) for 3 treatment cycles and that was followed by treatment with pertuzumab and trastuzumab FDC SC (PH FDC SC) for 3 treatment cycles (1 cycle = 21 days).

| | |
|----------------------------|--|
| Subject analysis set title | Arm A: Treatment With PH FDC SC (Cycles 4–6) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

This safety analysis population only includes adverse events that occurred in Arm A participants during treatment Cycles 4 to 6 when all Arm A participants were treated with PH FDC SC. In the Treatment Cross-Over Period of the study, participants randomized to Arm A first received treatment with pertuzumab IV and trastuzumab IV (P+H IV) for 3 treatment cycles and that was followed by treatment with pertuzumab and trastuzumab FDC SC (PH FDC SC) for 3 treatment cycles (1 cycle = 21 days).

| | |
|----------------------------|--|
| Subject analysis set title | Arm B: Treatment With PH FDC SC (Cycles 1–3) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

This safety analysis population only includes adverse events that occurred in Arm B participants during treatment Cycles 1 to 3 when all Arm B participants were treated with PH FDC SC. In the Treatment Cross-Over Period of the study, participants randomized to Arm B first received treatment with pertuzumab and trastuzumab FDC SC (PH FDC SC) for 3 treatment cycles and that was followed by treatment with pertuzumab IV and trastuzumab IV (P+H IV) for 3 treatment cycles (1 cycle = 21 days).

| | |
|----------------------------|---|
| Subject analysis set title | Arm B: Treatment With P+H IV (Cycles 4–6) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

This safety analysis population only includes adverse events that occurred in Arm B participants during treatment Cycles 4 to 6 when all Arm B participants were treated with P+H IV. In the Treatment Cross-Over Period of the study, participants randomized to Arm B first received treatment with pertuzumab and trastuzumab FDC SC (PH FDC SC) for 3 treatment cycles and that was followed by treatment with pertuzumab IV and trastuzumab IV (P+H IV) for 3 treatment cycles (1 cycle = 21 days).

| | |
|----------------------------|-------------------------------------|
| Subject analysis set title | P+H IV: Treatment Cross-Over Period |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

This safety analysis population includes all participants from Arms A and B who received up to 3 cycles (1 cycle = 21 days) of treatment with pertuzumab IV and trastuzumab IV (P+H IV) during the Treatment Cross-Over Period of the study.

| | |
|----------------------------|--|
| Subject analysis set title | PH FDC SC: Treatment Cross-Over Period |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

This safety analysis population includes all participants from Arms A and B who received up to 3 cycles (1 cycle = 21 days) of treatment with the pertuzumab and trastuzumab fixed-dose combination administered subcutaneously (PH FDC SC) during the Treatment Cross-Over Period of the study.

| | |
|----------------------------|---------------------------------------|
| Subject analysis set title | P+H IV: Treatment Continuation Period |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

This safety analysis population includes all participants from Arms A and B who, following completion of the Treatment Cross-Over Period, chose to receive pertuzumab IV and trastuzumab IV (P+H IV) during the Treatment Continuation Period for the remaining anti-HER2 treatment cycles (18 planned cycles in total, including pre-study neoadjuvant treatment).

| | |
|----------------------------|--|
| Subject analysis set title | PH FDC SC: Treatment Continuation Period |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

This safety analysis population includes all participants from Arms A and B who, following completion of the Treatment Cross-Over Period, chose to receive the pertuzumab and trastuzumab fixed-dose combination administered subcutaneously (PH FDC SC) during the Treatment Continuation Period for the remaining anti-HER2 treatment cycles (18 planned cycles in total, including pre-study neoadjuvant treatment).

Primary: Percentage of Participants by Their Preferred Method of Pertuzumab and Trastuzumab Administration, as Assessed in Question 1 of the Patient Preference Questionnaire (PPQ)

| | |
|-----------------|---|
| End point title | Percentage of Participants by Their Preferred Method of Pertuzumab and Trastuzumab Administration, as Assessed in Question 1 of the Patient Preference Questionnaire (PPQ) ^[1] |
|-----------------|---|

End point description:

Question 1 of the Patient Preference Questionnaire (PPQ) asked participants the following question: "All things considered, which method of administration did you prefer?" The three available options for a participant's response were: IV, SC, or No preference. A point estimate with associated exact Clopper-Pearson binomial 95% confidence interval (CI) was calculated only for the percentage of participants who preferred PH FDC SC (i.e., 95% CI values of 0.000000 to 999999 for IV and No Preference only indicate that they were not calculated). The modified Intent-to-Treat (mITT) population was analyzed, which included all randomized participants allocated to their randomized treatment arm, who received at least one dose by both SC and IV routes of administration during the Treatment Cross-over Period and subsequently answered at least Question 1 of the PPQ.

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

End point timeframe:

Cycle 6 Day 1 (each cycle is 21 days)

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: No formal hypothesis testing was planned for this study. The results are presented using descriptive statistics.

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|-----------------------------------|---------------------------------------|---------------------------------------|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 | 80 | 160 | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| SC Preference | 87.50 (78.21 to 93.84) | 82.50 (72.38 to 90.09) | 85.00 (78.51 to 90.15) | |
| IV Preference | 12.5 (0.000000 to 999999) | 15.0 (0.000000 to 999999) | 13.8 (0.000000 to 999999) | |
| No Preference | 0.0 (0.000000 to 999999) | 2.5 (0.000000 to 999999) | 1.3 (0.000000 to 999999) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants by Responses to the Strength of Their Preferred Method of Pertuzumab and Trastuzumab Administration, as Assessed in Question 2 of the Patient Preference Questionnaire (PPQ)

| | |
|-----------------|--|
| End point title | Percentage of Participants by Responses to the Strength of Their Preferred Method of Pertuzumab and Trastuzumab Administration, as Assessed in Question 2 of the Patient |
|-----------------|--|

End point description:

Question 1 of the Patient Preference Questionnaire (PPQ) was as follows: "All things considered, which method of administration did you prefer?" The available options for a participant's response were IV, SC, or No preference. In Question 2 of the PPQ, participants who reported a preference for one of the two administration routes in Question 1 of the PPQ were asked to rate the strength of their preference (very strong, fairly strong, not very strong). The modified ITT (mITT) Population was analyzed; for Question 2 of the PPQ, the number analyzed for the strength of SC or IV preference represents the participants who indicated in their responses to Question 1 of the PPQ that they preferred the SC or IV route of administration, respectively.

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

End point timeframe:

| |
|---------------------------------------|
| Cycle 6 Day 1 (each cycle is 21 days) |
|---------------------------------------|

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 | 78 | 158 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| SC Preference: Very Strong (n=70,66,136) | 68.6 | 66.7 | 67.6 | |
| SC Preference: Fairly Strong (n=70,66,136) | 24.3 | 25.8 | 25.0 | |
| SC Preference: Not Very Strong (n=70,66,136) | 7.1 | 7.6 | 7.4 | |
| IV Preference: Very Strong (n=10,12,22) | 40.0 | 66.7 | 54.5 | |
| IV Preference: Fairly Strong (n=10,12,22) | 10.0 | 8.3 | 9.1 | |
| IV Preference: Not Very Strong (n=10,12,22) | 50.0 | 25.0 | 36.4 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Responses from Participants to the Two Main Reasons for Their Preferred Method of Pertuzumab and Trastuzumab Administration, as Assessed in Question 3 of the Patient Preference Questionnaire (PPQ)

| | |
|-----------------|--|
| End point title | Percentage of Responses from Participants to the Two Main Reasons for Their Preferred Method of Pertuzumab and Trastuzumab Administration, as Assessed in Question 3 of the Patient Preference Questionnaire (PPQ) |
|-----------------|--|

End point description:

In Question 3 of the PPQ, participants who reported a preference for one of the two administration routes in Question 1 of the PPQ were asked to provide the two main reasons for their preference. The five available options for a participant's response were: Feels less emotionally distressing; Requires less time in the clinic; Lower level of injection-site pain; Feels more comfortable during administration; and Other reason. The modified ITT (mITT) population was analyzed; for Question 3, the number analyzed for the two main reasons for SC or IV preference represents the participants who indicated in their responses to Question 1 of the PPQ that they preferred the SC or IV route of administration, respectively.

| | |
|---------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Cycle 6 Day 1 (each cycle is 21 days) | |

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|--|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 | 78 | 158 | |
| Units: Percentage of responses | | | | |
| number (not applicable) | | | | |
| SC: Feels Less Emotionally Distressing | 14.7 | 18.0 | 16.3 | |
| SC: Requires Less Time in the Clinic | 42.0 | 42.4 | 42.2 | |
| SC: Lower Level of Injection-Site Pain | 9.8 | 12.9 | 11.3 | |
| SC: Feels More Comfortable During Administration | 28.7 | 23.0 | 25.9 | |
| SC: Other Reason | 4.9 | 3.6 | 4.3 | |
| IV: Feels Less Emotionally Distressing | 17.6 | 16.0 | 16.7 | |
| IV: Requires Less Time in the Clinic | 5.9 | 4.0 | 4.8 | |
| IV: Lower Level of Injection-Site Pain | 23.5 | 28.0 | 26.2 | |
| IV: Feels More Comfortable During Administration | 47.1 | 24.0 | 33.3 | |
| IV: Other Reason | 5.9 | 28.0 | 19.0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants by Their Level of Satisfaction with the Respective Methods of Administration (IV and SC), Question 1 of the Therapy Administration Satisfaction Questionnaire –Intravenous (TASQ-IV) and –Subcutaneous (TASQ-SC)

| | |
|-----------------|---|
| End point title | Percentage of Participants by Their Level of Satisfaction with the Respective Methods of Administration (IV and SC), Question 1 of the Therapy Administration Satisfaction Questionnaire –Intravenous (TASQ-IV) and –Subcutaneous (TASQ-SC) |
|-----------------|---|

End point description:

The Therapy Administration Satisfaction Questionnaire (TASQ) is a 12-item, patient-reported questionnaire measuring the impact of the mode of treatment administration (TASQ-IV for IV treatment and TASQ-SC for SC treatment) on five domains: Physical Impact, Psychological Impact, Impact on Activities of Daily Living, Convenience, and Satisfaction. The TASQ-IV/-SC was administered at treatment Cycles 3 and 6 according to the order of treatment received per arm during the Cross-Over Period. Question 1 of the TASQ-IV/TASQ-SC is one of two items in the Satisfaction domain, with participants providing their answers to the following question: "How satisfied or dissatisfied were you with the IV infusion/SC injection?" The five available options for a participant's response were: very satisfied, satisfied, neither satisfied nor dissatisfied, dissatisfied, and very dissatisfied. The modified Intent-to-Treat (mITT) population was analyzed.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Cycle 3 Day 1, Cycle 6 Day 1 (each cycle is 21 days) | |

| End point values | All Participants: TASQ-IV Completers | All Participants: TASQ-SC Completers | | |
|------------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 160 | 160 | | |
| Units: Participants | | | | |
| number (not applicable) | | | | |
| Very Satisfied | 25.6 | 57.5 | | |
| Satisfied | 41.9 | 30.6 | | |
| Neither Satisfied nor Dissatisfied | 25.6 | 4.4 | | |
| Dissatisfied | 5.6 | 1.9 | | |
| Very Dissatisfied | 1.3 | 4.4 | | |
| Did Not Answer Question | 0.0 | 1.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Scores of the Five Domains of the TASQ-IV and TASQ-SC (Satisfaction, Physical Impact, Psychological Impact, Impact on Activities of Daily Living, and Convenience) to Assess the Impact of IV and SC Routes of Administration

| | |
|-----------------|--|
| End point title | Mean Scores of the Five Domains of the TASQ-IV and TASQ-SC (Satisfaction, Physical Impact, Psychological Impact, Impact on Activities of Daily Living, and Convenience) to Assess the Impact of IV and SC Routes of Administration |
|-----------------|--|

End point description:

The TASQ is a 12-item, patient-reported questionnaire measuring the impact of the mode of treatment administration (TASQ-IV for IV treatment and TASQ-SC for SC treatment) on 5 domains: Physical Impact (3 items: Question [Q]2. Pain, Q3. Swelling, Q4. Redness), Psychological Impact (1 item: Q5. Feeling restricted), Impact on Activities of Daily Living (1 item: Q8. Lost/gained time), Convenience (2 items: Q6. Is it convenient?, Q7. Bothered by the amount of time?), and Satisfaction (2 items: Q1. How satisfied or dissatisfied are you with treatment?, Q12: Would you recommend the way you received the treatment?). In addition, 3 questions in the TASQ (Q9, Q10, Q11) are not part of the domains. Responses for the 3 domains that contain more than 1 item were scored from 0 to 100, with a higher score indicating a better outcome. Responses for the 2 domains with 1 item were scored from 1 to 5, with a higher score indicating a better outcome.

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

End point timeframe:

Cycle 3 Day 1, Cycle 6 Day 1 (each cycle is 21 days)

| End point values | All Participants: TASQ-IV Completers | All Participants: TASQ-SC Completers | | |
|--|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 160 | 160 | | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Satisfaction Domain | 64.3 (± 23.6) | 87.7 (± 17.5) | | |
| Physical Impact Domain | 86.5 (± 14.8) | 81.3 (± 15.4) | | |
| Psychological Impact Domain | 3.8 (± 1.2) | 4.6 (± 0.7) | | |
| Impact on Activities Daily Living Domain | 2.3 (± 0.9) | 3.9 (± 1.0) | | |
| Convenience Domain | 56.8 (± 26.0) | 90.0 (± 13.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants by Their Responses to Question 9 of the TASQ-IV and TASQ-SC, Assessing Whether Participants Receiving IV and SC Administration Have as Much Time as They Would Like to Talk to Their Nurse and/or Doctor About Their Illness

| | |
|-----------------|---|
| End point title | Percentage of Participants by Their Responses to Question 9 of the TASQ-IV and TASQ-SC, Assessing Whether Participants Receiving IV and SC Administration Have as Much Time as They Would Like to Talk to Their Nurse and/or Doctor About Their Illness |
|-----------------|---|

End point description:

The TASQ is a 12-item, patient-reported questionnaire measuring the impact of the mode of treatment administration (TASQ-IV for IV treatment and TASQ-SC for SC treatment) on 5 domains. In addition, 3 questions (Q.9-11) are not part of the domains. The TASQ-IV/-SC was administered at treatment Cycles 3 and 6 according to the order of treatment received per arm during the Cross-Over Period. Question 9 asked the participant, "When you receive the IV infusion/SC injection treatment, are you able to talk to your nurse and/or doctor as much as you would like about your illness?" There were five available response options: a) Yes, I had more than enough time to talk to my nurse and/or doctor; b) Yes, but I would have liked more time to talk to my nurse and/or doctor; c) It does not matter to me if I have time to talk to my nurse and/or doctor during my treatment; d) No, I did not have enough time to talk to my nurse and/or doctor; and e) No, I did not talk to my nurse and/or doctor at all.

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

End point timeframe:

Cycle 3 Day 1 and Cycle 6 Day 1 (each cycle is 21 days)

| End point values | All Participants: TASQ-IV Completers | All Participants: TASQ-SC Completers | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 160 | 160 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| a) Yes, I had enough time to talk | 82.5 | 90.0 | | |

| | | | | |
|--|-----|-----|--|--|
| b) Yes, but I would have liked more time to talk | 9.4 | 5.0 | | |
| c) It does not matter to me if I have time to talk | 5.0 | 3.1 | | |
| d) No, I did not have enough time to talk | 0.6 | 0.6 | | |
| e) No, I did not talk to my nurse/doctor | 2.5 | 0.0 | | |
| Patient did not answer question | 0.0 | 1.3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants by Their Responses to Question 10 of the TASQ-IV and TASQ-SC, Assessing Whether IV and SC Administration Have an Impact on the Amount of Time Participants Have to Talk to Their Nurse and/or Doctor About Their Illness

| | |
|-----------------|---|
| End point title | Percentage of Participants by Their Responses to Question 10 of the TASQ-IV and TASQ-SC, Assessing Whether IV and SC Administration Have an Impact on the Amount of Time Participants Have to Talk to Their Nurse and/or Doctor About Their Illness |
|-----------------|---|

End point description:

The Therapy Administration Satisfaction Questionnaire (TASQ) is a 12-item, patient-reported questionnaire measuring the impact of the mode of treatment administration (TASQ-IV for IV treatment and TASQ-SC for SC treatment) on 5 domains (questions [Q] 1 to 8 and Q12): Physical Impact, Psychological Impact, Impact on Activities of Daily Living, Convenience, and Satisfaction. In addition, 3 questions in the TASQ-IV/-SC (Q 9-11) are not part of the domains. The TASQ-IV/-SC were administered at treatment Cycles 3 and 6 according to the order of treatment received in each study arm during the Cross-Over Period. Question 10 of the TASQ-IV/-SC asked the participant "Does the IV infusion/SC injection impact the amount of time you have to talk to your nurse and/or doctor about your illness and other concerns?" There were two available options for the participant's response: Yes or No.

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

End point timeframe:

Cycle 3 Day 1 and Cycle 6 Day 1 (each cycle is 21 days)

| End point values | All Participants: TASQ-IV Completers | All Participants: TASQ-SC Completers | | |
|-----------------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 160 | 160 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Yes | 20.0 | 13.1 | | |
| No | 79.4 | 85.0 | | |
| Patient Did Not Answer Question | 0.6 | 1.9 | | |

Statistical analyses

Secondary: Percentage of Participants by Their Responses to Question 11 of the TASQ-IV and TASQ-SC, Assessing the Participants' Preferred Method for Receiving Cancer Treatment

| | |
|-----------------|--|
| End point title | Percentage of Participants by Their Responses to Question 11 of the TASQ-IV and TASQ-SC, Assessing the Participants' Preferred Method for Receiving Cancer Treatment |
|-----------------|--|

End point description:

The Therapy Administration Satisfaction Questionnaire (TASQ) is a 12-item, patient-reported questionnaire measuring the impact of the mode of treatment administration (TASQ-IV for IV treatment and TASQ-SC for SC treatment) on 5 domains (questions [Q] 1 to 8 and Q12): Physical Impact, Psychological Impact, Impact on Activities of Daily Living, Convenience, and Satisfaction. In addition, 3 questions in the TASQ-IV/-SC (Q 9-11) are not part of the domains. The TASQ-IV/-SC was administered at treatment Cycles 3 and 6 according to the order of treatment received during the Cross-Over Period. Question 11 of the TASQ-IV/-SC asked the participant, "There are two ways to get cancer treatment: a) IV infusion given through a port or small tube; b) SC (subcutaneous) injection in your thigh. Which would you prefer?" There were three available options for the participant's response: IV, SC, or No Preference.

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

End point timeframe:

Cycle 3 Day 1 and Cycle 6 Day 1 (each cycle is 21 days)

| End point values | All Participants: TASQ-IV Completers | All Participants: TASQ-SC Completers | | |
|-----------------------------------|--------------------------------------|--------------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 160 | 160 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Prefer IV Method | 11.9 | 9.4 | | |
| Prefer SC Method | 70.6 | 82.5 | | |
| No Preference | 11.9 | 5.6 | | |
| Patient Did Not Answer Question | 5.6 | 2.5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants by Their Choice of Treatment in the Treatment Continuation Period (PH FDC SC or P+H IV) and by Consistency of This Choice with Their Preferred Method of Administration Reported in Question 1 of the PPQ

| | |
|-----------------|--|
| End point title | Percentage of Participants by Their Choice of Treatment in the Treatment Continuation Period (PH FDC SC or P+H IV) and by Consistency of This Choice with Their Preferred Method of Administration Reported in Question 1 of the PPQ |
|-----------------|--|

End point description:

At treatment Cycle 7, participants were expected to select the study treatment formulation (PH FDC SC or P+H IV) to complete their 18 cycles of neo/adjuvant HER2-targeted treatment after completion of the Treatment Cross-over Period. Additionally, for each participant's preference category (SC, IV, and No

preference) as per the question 1 of the patient preference questionnaire (PPQ), the percentage of participants who selected each treatment administration route for the Treatment Continuation Period (PH FDC SC or P+H IV) was summarized.

| | |
|---------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Cycle 7 Day 1 (each cycle is 21 days) | |

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 | 80 | 160 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Chose SC for Treatment Continuation | 88.8 | 85.0 | 86.9 | |
| Chose IV for Treatment Continuation | 11.3 | 15.0 | 13.1 | |
| Preferred SC per PPQ & Chose SC for Continuation | 87.5 | 82.5 | 85.0 | |
| Preferred SC per PPQ & Chose IV for Continuation | 0.0 | 0.0 | 0.0 | |
| Preferred IV per PPQ & Chose SC for Continuation | 1.3 | 0.0 | 0.6 | |
| Preferred IV per PPQ & Chose IV for Continuation | 11.3 | 15.0 | 13.1 | |
| No Preference per PPQ & Chose SC for Continuation | 0.0 | 2.5 | 1.3 | |
| No Preference per PPQ & Chose IV for Continuation | 0.0 | 0.0 | 0.0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Treatment Administration Activities According to Healthcare Professionals' Responses on Perception of Time by Treatment Cycle, Question 1 of the Healthcare Professional Questionnaire (HCPQ) - Treatment Room

| | |
|-----------------|--|
| End point title | Duration of Treatment Administration Activities According to Healthcare Professionals' Responses on Perception of Time by Treatment Cycle, Question 1 of the Healthcare Professional Questionnaire (HCPQ) - Treatment Room |
|-----------------|--|

End point description:

The Healthcare Professional Questionnaire (HCPQ)-Treatment Room Question 1 was completed at each treatment cycle of the Treatment Cross-Over Period by the healthcare professionals (HCPs) who administered treatment to the study's participants. HCPs responded to the following parts of Question 1 that sought to evaluate the amount of time it took to complete activities related to treatment administration: "If new IV access was needed for this cycle of treatment, please indicate what type of IV access was provided (central venous catheter [CVC], peripherally inserted central catheter [PICC], or peripheral vein cannulation [PVC]) and how long (in minutes) this took to set up (only for participants receiving IV treatment)? How long (in minutes) did it take to administer the treatment, i.e. total infusion duration? How long (in minutes) was the patient in the Treatment Room for in total?" The value '999999' indicates 0 participants were analyzed.

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

End point timeframe:

Day 1 of Cycles (Cyc) 1-6 (each cycle is 21 days)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | | |
|---|---------------------------------------|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 80 | 80 | | |
| Units: minutes | | | | |
| median (full range (min-max)) | | | | |
| Cyc 1. Time for CVC Set Up (IV Only; n=4,0) | 5.0 (4 to 6) | 999999 (999999 to 999999) | | |
| Cyc 1. Time for PICC Set Up (IV Only; n=1,0) | 5.0 (5 to 5) | 999999 (999999 to 999999) | | |
| Cyc 1. Time for PVC Set Up (IV Only; n=50,0) | 5.0 (1 to 40) | 999999 (999999 to 999999) | | |
| Cyc 1. Time Taken to Administer Treatment(n=79,79) | 150.0 (60 to 396) | 8.0 (2 to 17) | | |
| Cyc 1. Time Patient Was in Treatment Room(n=79,79) | 300.0 (90 to 450) | 50.0 (8 to 240) | | |
| Cyc 2. Time for CVC Set Up (IV Only; n=4,0) | 5.0 (3 to 5) | 999999 (999999 to 999999) | | |
| Cyc 2. Time for PICC Set Up (IV Only; n=1,0) | 3.0 (3 to 3) | 999999 (999999 to 999999) | | |
| Cyc 2. Time for PVC Set Up (IV Only; n=48,0) | 5.0 (1 to 20) | 999999 (999999 to 999999) | | |
| Cyc 2. Time Taken to Administer Treatment(n=77,80) | 90.0 (8 to 260) | 8.0 (5 to 20) | | |
| Cyc 2. Time Patient Was in Treatment Room(n=77,78) | 153.0 (30 to 342) | 40.0 (8 to 225) | | |
| Cyc 3. Time for CVC Set Up (IV Only; n=5,0) | 5.0 (3 to 10) | 999999 (999999 to 999999) | | |
| Cyc 3. Time for PICC Set Up (IV Only; n=1,0) | 3.0 (3 to 3) | 999999 (999999 to 999999) | | |
| Cyc 3. Time for PVC Set Up (IV Only; n=48,0) | 5.0 (1 to 30) | 999999 (999999 to 999999) | | |
| Cyc 3. Time Taken to Administer Treatment(n=79,80) | 70.0 (30 to 240) | 7.5 (4 to 16) | | |
| Cyc 3. Time Patient Was in Treatment Room(n=79,79) | 150.0 (105 to 330) | 36.0 (5 to 327) | | |
| Cyc 4. Time for CVC Set Up (IV Only; n=0,7) | 999999 (999999 to 999999) | 5.0 (2 to 10) | | |
| Cyc 4. Time for PICC Set Up (IV Only; n=0,1) | 999999 (999999 to 999999) | 42.0 (42 to 42) | | |
| Cyc 4. Time for PVC Set Up (IV Only; n=0,36) | 999999 (999999 to 999999) | 5.0 (1 to 20) | | |

| | | | | |
|--|------------------------------|------------------------------|--|--|
| Cyc 4. Time Taken to Administer Treatment(n=80,77) | 8.0 (4 to 12) | 60.0 (30 to 210) | | |
| Cyc 4. Time Patient Was in Treatment Room(n=78,77) | 45.0 (1 to 185) | 150.0 (80 to 480) | | |
| Cyc 5. Time for CVC Set Up (IV Only; n=0,5) | 999999 (999999 to 999999) | 3.0 (2 to 10) | | |
| Cyc 5. Time for PICC Set Up (IV Only; n=0,1) | 999999 (999999 to 999999) | 10.0 (10 to 10) | | |
| Cyc 5. Time for PVC Set Up (IV Only; n=0,38) | 999999 (999999 to 999999) | 5.0 (1 to 20) | | |
| Cyc 5. Time Taken to Administer Treatment(n=79,77) | 8.0 (3 to 14) | 83.0 (30 to 200) | | |
| Cyc 5. Time Patient Was in Treatment Room(n=79,77) | 33.0 (8 to 135) | 150.0 (95 to 343) | | |
| Cyc 6. Time for CVC Set Up (IV Only; n=0,6) | 999999 (999999 to 999999) | 10.0 (1 to 91) | | |
| Cyc 6. Time for PICC Set Up (IV Only; n=0,0) | 999999 (999999 to 999999) | 999999 (999999 to 999999) | | |
| Cyc 6. Time for PVC Set Up (IV Only; n=0,43) | 999999 (999999 to 999999) | 5.0 (1 to 60) | | |
| Cyc 6. Time Taken to Administer Treatment(n=79,80) | 7.0 (3 to 11) | 60.0 (5 to 275) | | |
| Cyc 6. Time Patient Was in Treatment Room(n=79,80) | 35.0 (10 to 150) | 130.0 (45 to 330) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Healthcare Professionals (HCPs) by Their Responses on Perception of Impact of PH FDC SC on Clinical Management and Clinical Efficiency, Question 2 of the HCPQ - Treatment Room

| | |
|-----------------|---|
| End point title | Percentage of Healthcare Professionals (HCPs) by Their Responses on Perception of Impact of PH FDC SC on Clinical Management and Clinical Efficiency, Question 2 of the HCPQ - Treatment Room |
|-----------------|---|

End point description:

HCPs who administered study treatment responded at Cycle 6 of the Treatment Cross-Over Period to the following HCPQ-Treatment Room Question 2: "If all P+H IV infusions are switched to FDC SC injections, please indicate how strongly you agree or disagree with each of the following statements: a) Patients will be moved outside of infusion unit to receive FDC SC; b) FDC SC route will allow more flexible scheduling; c) More patients will be treated in the infusion unit; d) Waiting list for any P+H IV treatment at the infusion unit will be reduced; e) Staff resources will be redistributed to other departments of the hospital; f) There will still be sufficient interaction time between HCPs and patients; g) Staff will spend more time for further education/development; h) Staff will dedicate more time attending to administrative tasks for Perjeta-Herceptin patients; i) Patients will spend less time in the care unit; j) Administration by FDC SC injection is preferred by patients."

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

End point timeframe:

Day 1 of Cycle 6 (each cycle is 21 days)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Healthcare Professionals | |
|---------------------------------|---------------------------------------|---------------------------------------|---------------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 | 80 | 159 | |
| Units: Percentage of HCPs | | | | |
| number (not applicable) | | | | |
| Statement a): Strongly Disagree | 11.4 | 21.3 | 16.4 | |
| Statement a): Disagree | 12.7 | 17.5 | 15.1 | |
| Statement a): Neutral | 8.9 | 3.8 | 6.3 | |
| Statement a): Agree | 26.6 | 16.3 | 21.4 | |
| Statement a): Strongly Agree | 22.8 | 22.5 | 22.6 | |
| Statement a): Not Applicable | 13.9 | 11.3 | 12.6 | |
| Statement a): Answer Missing | 3.8 | 7.5 | 5.7 | |
| Statement b): Strongly Disagree | 0.0 | 6.3 | 3.1 | |
| Statement b): Disagree | 7.6 | 10.0 | 8.8 | |
| Statement b): Neutral | 10.1 | 7.5 | 8.8 | |
| Statement b): Agree | 29.1 | 27.5 | 28.3 | |
| Statement b): Strongly Agree | 49.4 | 41.3 | 45.3 | |
| Statement b): Not Applicable | 0.0 | 0.0 | 0.0 | |
| Statement b): Answer Missing | 3.8 | 7.5 | 5.7 | |
| Statement c): Strongly Disagree | 1.3 | 3.8 | 2.5 | |
| Statement c): Disagree | 7.6 | 7.5 | 7.5 | |
| Statement c): Neutral | 17.7 | 12.5 | 15.1 | |
| Statement c): Agree | 29.1 | 31.3 | 30.2 | |
| Statement c): Strongly Agree | 36.7 | 37.5 | 37.1 | |
| Statement c): Not Applicable | 3.8 | 0.0 | 1.9 | |
| Statement c): Answer Missing | 3.8 | 7.5 | 5.7 | |
| Statement d): Strongly Disagree | 1.3 | 7.5 | 4.4 | |
| Statement d): Disagree | 8.9 | 7.5 | 8.2 | |
| Statement d): Neutral | 17.7 | 11.3 | 14.5 | |
| Statement d): Agree | 29.1 | 26.3 | 27.7 | |
| Statement d): Strongly Agree | 36.7 | 33.8 | 35.2 | |
| Statement d): Not Applicable | 2.5 | 5.0 | 3.8 | |
| Statement d): Answer Missing | 3.8 | 8.8 | 6.3 | |
| Statement e): Strongly Disagree | 15.2 | 10.0 | 12.6 | |
| Statement e): Disagree | 16.5 | 22.5 | 19.5 | |
| Statement e): Neutral | 17.7 | 22.5 | 20.1 | |
| Statement e): Agree | 19.0 | 11.3 | 15.1 | |
| Statement e): Strongly Agree | 20.3 | 18.8 | 19.5 | |
| Statement e): Not Applicable | 7.6 | 6.3 | 6.9 | |
| Statement e): Answer Missing | 3.8 | 8.8 | 6.3 | |
| Statement f): Strongly Disagree | 0.0 | 3.8 | 1.9 | |
| Statement f): Disagree | 6.3 | 3.8 | 5.0 | |
| Statement f): Neutral | 15.2 | 16.3 | 15.7 | |
| Statement f): Agree | 31.6 | 32.5 | 32.1 | |
| Statement f): Strongly Agree | 43.0 | 35.0 | 39.0 | |
| Statement f): Not Applicable | 0.0 | 0.0 | 0.0 | |

| | | | | |
|---------------------------------|------|------|------|--|
| Statement f): Answer Missing | 3.8 | 8.8 | 6.3 | |
| Statement g): Strongly Disagree | 0.0 | 5.0 | 2.5 | |
| Statement g): Disagree | 7.6 | 11.3 | 9.4 | |
| Statement g): Neutral | 31.6 | 23.8 | 27.7 | |
| Statement g): Agree | 20.3 | 22.5 | 21.4 | |
| Statement g): Strongly Agree | 35.4 | 27.5 | 31.4 | |
| Statement g): Not Applicable | 1.3 | 2.5 | 1.9 | |
| Statement g): Answer Missing | 3.8 | 7.5 | 5.7 | |
| Statement h): Strongly Disagree | 1.3 | 5.0 | 3.1 | |
| Statement h): Disagree | 11.4 | 16.3 | 13.8 | |
| Statement h): Neutral | 25.3 | 23.8 | 24.5 | |
| Statement h): Agree | 24.1 | 16.3 | 20.1 | |
| Statement h): Strongly Agree | 32.9 | 27.5 | 30.2 | |
| Statement h): Not Applicable | 1.3 | 3.8 | 2.5 | |
| Statement h): Answer Missing | 3.8 | 7.5 | 5.7 | |
| Statement i): Strongly Disagree | 0.0 | 0.0 | 0.0 | |
| Statement i): Disagree | 6.3 | 3.8 | 5.0 | |
| Statement i): Neutral | 1.3 | 5.0 | 3.1 | |
| Statement i): Agree | 27.8 | 22.5 | 25.2 | |
| Statement i): Strongly Agree | 60.8 | 60.0 | 60.4 | |
| Statement i): Not Applicable | 0.0 | 0.0 | 0.0 | |
| Statement i): Answer Missing | 3.8 | 8.8 | 6.3 | |
| Statement j): Strongly Disagree | 0.0 | 0.0 | 0.0 | |
| Statement j): Disagree | 8.9 | 1.3 | 5.0 | |
| Statement j): Neutral | 10.1 | 15.0 | 12.6 | |
| Statement j): Agree | 22.8 | 26.3 | 24.5 | |
| Statement j): Strongly Agree | 53.2 | 47.5 | 50.3 | |
| Statement j): Not Applicable | 1.3 | 1.3 | 1.3 | |
| Statement j): Answer Missing | 3.8 | 8.8 | 6.3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Healthcare Professionals (HCPs) by Their Responses on Perception of Time/Resource Use and Convenience of Each Study Regimen, Questions 3 to 7 of the HCPQ - Treatment Room

| | |
|-----------------|--|
| End point title | Percentage of Healthcare Professionals (HCPs) by Their Responses on Perception of Time/Resource Use and Convenience of Each Study Regimen, Questions 3 to 7 of the HCPQ - Treatment Room |
|-----------------|--|

End point description:

Healthcare professionals (HCPs) who administered study treatment responded at Cycle 6 of the Treatment Cross-Over Period to the following HCPQ-Treatment Room Questions (Q) 3 to 7: "Looking back over the Perjeta-Herceptin treatment sessions, please indicate based on your opinion which administration method: Q3. Which Method Was Most Convenient for the Patient? Q4. Which Method Was Best for Optimizing Patient Care in Your Centre? Q5. Which Method Took the Least Time from Start to Finish of Administration? Q6. Which Method Required the Least Resource Use for Administration? Q7. Which Method Was Preferred by Patients?" The four available response options were: P+H IV, FDC SC, No Difference, and Unsure.

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

End point timeframe:

Day 1 of Cycle 6 (each cycle is 21 days)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Healthcare Professionals | |
|-----------------------------|---------------------------------------|---------------------------------------|---------------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 | 80 | 159 | |
| Units: Percentage of HCPs | | | | |
| number (not applicable) | | | | |
| Q3. Answer: FDC SC | 88.6 | 85.0 | 86.8 | |
| Q3. Answer: P+H IV | 6.3 | 1.3 | 3.8 | |
| Q3. Answer: No Difference | 2.5 | 5.0 | 3.8 | |
| Q3. Answer: Unsure | 0.0 | 7.5 | 3.8 | |
| Q3. Answer: Missing | 2.5 | 1.3 | 1.9 | |
| Q4. Answer: FDC SC | 79.7 | 78.8 | 79.2 | |
| Q4. Answer: P+H IV | 3.8 | 1.3 | 2.5 | |
| Q4. Answer: No Difference | 12.7 | 12.5 | 12.6 | |
| Q4. Answer: Unsure | 1.3 | 6.3 | 3.8 | |
| Q4. Answer: Missing | 2.5 | 1.3 | 1.9 | |
| Q5. Answer: FDC SC | 94.9 | 96.3 | 95.6 | |
| Q5. Answer: P+H IV | 0.0 | 0.0 | 0.0 | |
| Q5. Answer: No Difference | 2.5 | 2.5 | 2.5 | |
| Q5. Answer: Unsure | 0.0 | 0.0 | 0.0 | |
| Q5. Answer: Missing | 2.5 | 1.3 | 1.9 | |
| Q6. Answer: FDC SC | 83.5 | 88.8 | 86.2 | |
| Q6. Answer: P+H IV | 0.0 | 1.3 | 0.6 | |
| Q6. Answer: No Difference | 13.9 | 8.8 | 11.3 | |
| Q6. Answer: Unsure | 0.0 | 0.0 | 0.0 | |
| Q6. Answer: Missing | 2.5 | 1.3 | 1.9 | |
| Q7. Answer: FDC SC | 77.2 | 77.5 | 77.4 | |
| Q7. Answer: P+H IV | 7.6 | 5.0 | 6.3 | |
| Q7. Answer: No Difference | 2.5 | 2.5 | 2.5 | |
| Q7. Answer: Unsure | 10.1 | 13.8 | 11.9 | |
| Q7. Answer: Missing | 2.5 | 1.3 | 1.9 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Healthcare Professionals (HCPs) by Their Responses to Question 8 of the HCPQ - Treatment Room

| | |
|-----------------|---|
| End point title | Percentage of Healthcare Professionals (HCPs) by Their Responses to Question 8 of the HCPQ - Treatment Room |
|-----------------|---|

End point description:

Healthcare professionals (HCPs) who administered study treatment responded at Cycle 6 of the Treatment Cross-Over Period to the following HCPQ-Treatment Room Question 8: "How frequently would you offer or recommend FDC SC administration to your patients in the future?" The three available

response options were: Always, Sometimes, and Never.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 of Cycle 6 (each cycle is 21 days) | |

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Healthcare Professionals | |
|-----------------------------|---------------------------------------|---------------------------------------|---------------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 | 80 | 159 | |
| Units: Percentage of HCPs | | | | |
| number (not applicable) | | | | |
| Always | 69.6 | 65.0 | 67.3 | |
| Sometimes | 26.6 | 33.8 | 30.2 | |
| Never | 1.3 | 0.0 | 0.6 | |
| Missing | 2.5 | 1.3 | 1.9 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Treatment Preparation According to Healthcare Professionals' Responses on Perception of Time by Treatment Cycle, Question 1 of the HCPQ - Drug Preparation Room

| | |
|-----------------|---|
| End point title | Duration of Treatment Preparation According to Healthcare Professionals' Responses on Perception of Time by Treatment Cycle, Question 1 of the HCPQ - Drug Preparation Room |
|-----------------|---|

End point description:

The Healthcare Professional Questionnaire (HCPQ)-Drug Preparation Room Question 1 was completed at each treatment cycle of the Treatment Cross-Over Period by the healthcare professionals (HCPs) within the pharmacy/drug preparation area where pertuzumab IV and trastuzumab IV and pertuzumab and trastuzumab FDC SC were prepared and dispensed for treating the study's participants. HCPs responded to the following question: "How long (in minutes) did it take to prepare the treatment for use?"

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 of Cycles 1-6 (each cycle is 21 days) | |

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | | |
|-------------------------------|---------------------------------------|---------------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 80 | 80 | | |
| Units: minutes | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1 (n = 80, 79) | 20.0 (3 to 60) | 5.0 (1 to 50) | | |
| Cycle 2 (n = 79, 80) | 20.0 (3 to 60) | 5.0 (1 to 30) | | |
| Cycle 3 (n = 80, 79) | 17.5 (3 to 90) | 5.0 (1 to 40) | | |

| | | | | |
|----------------------|---------------|----------------|--|--|
| Cycle 4 (n = 80, 80) | 5.0 (1 to 30) | 15.0 (3 to 49) | | |
| Cycle 5 (n = 80, 79) | 5.0 (1 to 35) | 15.0 (3 to 50) | | |
| Cycle 6 (n = 80, 78) | 5.0 (1 to 40) | 15.0 (3 to 50) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Healthcare Professionals (HCPs) by Their Responses on Perception of Impact of PH FDC SC on Clinical Management and Clinical Efficiency, Question 2 of the HCPQ - Drug Preparation Room

| | |
|-----------------|--|
| End point title | Percentage of Healthcare Professionals (HCPs) by Their Responses on Perception of Impact of PH FDC SC on Clinical Management and Clinical Efficiency, Question 2 of the HCPQ - Drug Preparation Room |
|-----------------|--|

End point description:

Healthcare professionals (HCPs) who prepared study treatment within the pharmacy/drug preparation area responded at Cycle 6 of the Treatment Cross-Over Period to the following HCPQ-Drug Preparation Room Question 2: "If all P+H IV infusions are switched to FDC SC injections, please indicate how strongly you agree or disagree with each of the following statements: a) Staff will have increased availability for other tasks in the pharmacy; b) Administrative procedures around FDC SC will require less time; c) FDC SC formulations will provide more flexibility for staff in managing their workload; d) Due to ready-to-use FDC SC formulations, potential dosing errors will be avoided; e) Due to ready-to-use FDC SC formulations, there will be less drug wastage; f) Without having to reconstitute the drug, less storage space for FDC SC related supplies will be required in the pharmacy; g) Preparation procedures and associated time staff time commitment will be reduced."

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

End point timeframe:

Day 1 of Cycle 6 (each cycle is 21 days)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Healthcare Professionals | |
|---------------------------------|---------------------------------|---------------------------------|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 | 80 | 160 | |
| Units: Percentage of HCPs | | | | |
| number (not applicable) | | | | |
| Statement a): Strongly Disagree | 1.3 | 1.3 | 1.3 | |
| Statement a): Disagree | 1.3 | 0.0 | 0.6 | |
| Statement a): Neutral | 8.8 | 6.3 | 7.5 | |
| Statement a): Agree | 28.8 | 28.8 | 28.8 | |
| Statement a): Strongly Agree | 52.5 | 48.8 | 50.6 | |
| Statement a): Not Applicable | 3.8 | 1.3 | 2.5 | |
| Statement a): Answer Missing | 3.8 | 13.8 | 8.8 | |
| Statement b): Strongly Disagree | 8.8 | 2.5 | 5.6 | |
| Statement b): Disagree | 3.8 | 3.8 | 3.8 | |
| Statement b): Neutral | 16.3 | 12.5 | 14.4 | |
| Statement b): Agree | 17.5 | 18.8 | 18.1 | |
| Statement b): Strongly Agree | 46.3 | 46.3 | 46.3 | |
| Statement b): Not Applicable | 2.5 | 2.5 | 2.5 | |
| Statement b): Answer Missing | 5.0 | 13.8 | 9.4 | |

| | | | | |
|---------------------------------|------|------|------|--|
| Statement c): Strongly Disagree | 0.0 | 1.3 | 0.6 | |
| Statement c): Disagree | 0.0 | 1.3 | 0.6 | |
| Statement c): Neutral | 15.0 | 11.3 | 13.1 | |
| Statement c): Agree | 28.8 | 23.8 | 26.3 | |
| Statement c): Strongly Agree | 50.0 | 47.5 | 48.8 | |
| Statement c): Not Applicable | 1.3 | 1.3 | 1.3 | |
| Statement c): Answer Missing | 5.0 | 6.3 | 9.4 | |
| Statement d): Strongly Disagree | 1.3 | 1.3 | 1.3 | |
| Statement d): Disagree | 1.3 | 6.3 | 3.8 | |
| Statement d): Neutral | 5.0 | 6.3 | 5.6 | |
| Statement d): Agree | 26.3 | 20.0 | 23.1 | |
| Statement d): Strongly Agree | 60.0 | 52.5 | 56.3 | |
| Statement d): Not Applicable | 1.3 | 1.3 | 1.3 | |
| Statement d): Answer Missing | 5.0 | 12.5 | 8.8 | |
| Statement e): Strongly Disagree | 1.3 | 1.3 | 1.3 | |
| Statement e): Disagree | 1.3 | 2.5 | 1.9 | |
| Statement e): Neutral | 11.3 | 6.3 | 8.8 | |
| Statement e): Agree | 21.3 | 22.5 | 21.9 | |
| Statement e): Strongly Agree | 58.8 | 51.3 | 55.0 | |
| Statement e): Not Applicable | 1.3 | 2.5 | 1.9 | |
| Statement e): Answer Missing | 5.0 | 13.8 | 9.4 | |
| Statement f): Strongly Disagree | 0.0 | 1.3 | 0.6 | |
| Statement f): Disagree | 3.8 | 5.0 | 4.4 | |
| Statement f): Neutral | 16.3 | 7.5 | 11.9 | |
| Statement f): Agree | 20.0 | 28.8 | 24.4 | |
| Statement f): Strongly Agree | 53.8 | 42.5 | 48.1 | |
| Statement f): Not Applicable | 1.3 | 1.3 | 1.3 | |
| Statement f): Answer Missing | 5.0 | 13.8 | 9.4 | |
| Statement g): Strongly Disagree | 0.0 | 1.3 | 0.6 | |
| Statement g): Disagree | 0.0 | 0.0 | 0.0 | |
| Statement g): Neutral | 8.8 | 5.0 | 6.9 | |
| Statement g): Agree | 30.0 | 32.5 | 31.3 | |
| Statement g): Strongly Agree | 52.5 | 45.0 | 48.8 | |
| Statement g): Not Applicable | 3.8 | 2.5 | 3.1 | |
| Statement g): Answer Missing | 5.0 | 13.8 | 9.4 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Healthcare Professionals (HCPs) by Their Responses on Perception of Time/Resource Use of Each Study Regimen, Questions 3 and 4 of the HCPQ - Drug Preparation Room

| | |
|-----------------|--|
| End point title | Percentage of Healthcare Professionals (HCPs) by Their Responses on Perception of Time/Resource Use of Each Study Regimen, Questions 3 and 4 of the HCPQ - Drug Preparation Room |
|-----------------|--|

End point description:

Healthcare professionals (HCPs) who prepared study treatment within the pharmacy/drug preparation area responded at Cycle 6 of the Treatment Cross-Over Period to the following HCPQ-Drug Preparation Room Questions 3 and 4: "Looking back over the Perjeta-Herceptin treatment sessions, please indicate

based on your opinion which administration method: Q3. Was quickest from start to end of preparation to finish of administration (excluding observation period)?; Q4. Required less resource use for preparation and administration, for example nursing time, facility costs, equipment etc?" The three available response options were: P+H IV, FDC SC, and No Difference.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Day 1 of Cycle 6 (each cycle is 21 days) | |

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Healthcare Professionals | |
|-----------------------------|---------------------------------------|---------------------------------------|---------------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 | 80 | 160 | |
| Units: Percentage of HCPs | | | | |
| number (not applicable) | | | | |
| Q3. Answer: FDC SC | 92.5 | 82.5 | 87.5 | |
| Q3. Answer: P+H IV | 0.0 | 1.3 | 0.6 | |
| Q3. Answer: No Difference | 1.3 | 1.3 | 1.3 | |
| Q3. Answer: Missing | 6.3 | 15.0 | 10.6 | |
| Q4. Answer: FDC SC | 93.8 | 80.0 | 86.9 | |
| Q4. Answer: P+H IV | 0.0 | 0.0 | 0.0 | |
| Q4. Answer: No Difference | 0.0 | 5.0 | 2.5 | |
| Q4. Answer: Missing | 6.3 | 15.0 | 10.6 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in Health-Related Quality of Life (HRQoL) as Assessed by the Global Health Status (GHS)/HRQoL Scale Score of the the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire 30 (EORTC QLQ-C30)

| | |
|-----------------|---|
| End point title | Change From Baseline Over Time in Health-Related Quality of Life (HRQoL) as Assessed by the Global Health Status (GHS)/HRQoL Scale Score of the the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire 30 (EORTC QLQ-C30) |
|-----------------|---|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years) | |

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[2] | 80 ^[3] | 159 ^[4] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 71.62 (± 17.98) | 76.77 (± 15.22) | 74.21 (± 16.79) | |
| Change from BL at Cycle 3 Day 1 (n=77,80,157) | 0.54 (± 16.63) | 0.00 (± 14.88) | 0.27 (± 15.72) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | 1.10 (± 20.25) | -1.16 (± 16.44) | -0.05 (± 18.38) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | 2.82 (± 16.30) | 1.76 (± 17.87) | 2.29 (± 17.05) | |
| Change from BL at 1.5 Years (n=72,74,146) | 7.18 (± 21.73) | 6.42 (± 16.92) | 6.79 (± 19.38) | |
| Change from BL at 2 Years (n=73,73,146) | 6.16 (± 19.45) | 4.11 (± 17.46) | 5.14 (± 18.45) | |
| Change from BL at 3 Years (n=68,65,133) | 7.23 (± 16.85) | 6.54 (± 20.12) | 6.89 (± 18.45) | |

Notes:

[2] - n = participants with non-missing data at baseline and a given timepoint.

[3] - n = participants with non-missing data at baseline and a given timepoint.

[4] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Physical Functioning Scale Score of the EORTC QLQ-C30

| | |
|-----------------|---|
| End point title | Change From Baseline Over Time in the Physical Functioning Scale Score of the EORTC QLQ-C30 |
|-----------------|---|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[5] | 80 ^[6] | 159 ^[7] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 84.22 (± 14.91) | 88.08 (± 13.86) | 86.16 (± 14.48) | |
| Change from BL at Cycle 3 Day 1 (n=79,80,159) | 1.77 (± 12.97) | -0.42 (± 11.09) | 0.67 (± 12.08) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | 1.93 (± 16.61) | 0.51 (± 12.11) | 1.20 (± 14.46) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | 3.85 (± 13.65) | 1.22 (± 17.69) | 2.54 (± 15.79) | |
| Change from BL at 1.5 Years (n=72,74,146) | 5.44 (± 17.29) | 4.05 (± 14.08) | 4.74 (± 15.71) | |
| Change from BL at 2 Years (n=73,73,146) | 4.38 (± 18.57) | 3.56 (± 13.84) | 3.97 (± 16.32) | |
| Change from BL at 3 Years (n=68,65,133) | 3.33 (± 13.99) | 1.64 (± 15.41) | 2.51 (± 14.67) | |

Notes:

[5] - n = participants with non-missing data at baseline and a given timepoint.

[6] - n = participants with non-missing data at baseline and a given timepoint.

[7] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Role Functioning Scale Score of the EORTC QLQ-C30

| | |
|-----------------|---|
| End point title | Change From Baseline Over Time in the Role Functioning Scale Score of the EORTC QLQ-C30 |
|-----------------|---|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[8] | 80 ^[9] | 159 ^[10] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 79.54 (± 25.45) | 77.08 (± 26.17) | 78.30 (± 25.76) | |
| Change from BL at Cycle 3 Day 1 (n=79,80,159) | 3.80 (± 24.01) | 9.58 (± 26.49) | 6.71 (± 25.37) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | 6.36 (± 24.03) | 8.44 (± 28.10) | 7.42 (± 26.12) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | 6.81 (± 24.00) | 12.44 (± 34.24) | 9.62 (± 29.60) | |
| Change from BL at 1.5 Years (n=72,74,146) | 9.49 (± 29.31) | 16.89 (± 30.41) | 13.24 (± 30.00) | |
| Change from BL at 2 Years (n=73,73,146) | 11.64 (± 29.22) | 10.96 (± 31.08) | 11.30 (± 30.07) | |
| Change from BL at 3 Years (n=68,65,133) | 8.09 (± 26.78) | 12.82 (± 31.43) | 10.40 (± 29.13) | |

Notes:

[8] - n = participants with non-missing data at baseline and a given timepoint.

[9] - n = participants with non-missing data at baseline and a given timepoint.

[10] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Emotional Functioning Scale Score of the EORTC QLQ-C30

| | |
|-----------------|--|
| End point title | Change From Baseline Over Time in the Emotional Functioning Scale Score of the EORTC QLQ-C30 |
|-----------------|--|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[11] | 80 ^[12] | 159 ^[13] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 82.07 (± 16.99) | 82.08 (± 18.52) | 82.08 (± 17.72) | |
| Change from BL at Cycle 3 Day 1 (n=78,80,158) | -1.28 (± 15.26) | 1.35 (± 16.53) | 0.05 (± 15.92) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | 0.99 (± 20.04) | -0.32 (± 17.42) | 0.32 (± 18.70) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | -1.17 (± 15.77) | 2.46 (± 22.77) | 0.65 (± 19.60) | |
| Change from BL at 1.5 Years (n=72,74,146) | 0.93 (± 23.05) | 3.94 (± 21.95) | 2.45 (± 22.47) | |
| Change from BL at 2 Years (n=73,73,146) | 2.74 (± 21.61) | 0.99 (± 25.89) | 1.86 (± 23.78) | |
| Change from BL at 3 Years (n=68,65,133) | 3.55 (± 21.08) | 1.15 (± 26.43) | 2.38 (± 23.78) | |

Notes:

[11] - n = participants with non-missing data at baseline and a given timepoint.

[12] - n = participants with non-missing data at baseline and a given timepoint.

[13] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Cognitive Functioning Scale Score of the EORTC QLQ-C30

| | |
|-----------------|--|
| End point title | Change From Baseline Over Time in the Cognitive Functioning Scale Score of the EORTC QLQ-C30 |
|-----------------|--|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[14] | 80 ^[15] | 159 ^[16] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 85.86 (± 17.92) | 84.58 (± 18.90) | 85.22 (± 18.37) | |
| Change from BL at Cycle 3 Day 1 (n=78,80,158) | -0.64 (± 17.08) | -1.25 (± 21.18) | -0.95 (± 19.21) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | -3.29 (± 18.86) | -1.69 (± 21.94) | -2.47 (± 20.44) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | -7.75 (± 21.79) | -1.64 (± 23.09) | -4.69 (± 22.58) | |
| Change from BL at 1.5 Years (n=72,74,146) | -3.47 (± 20.16) | -0.45 (± 22.41) | -1.94 (± 21.31) | |
| Change from BL at 2 Years (n=73,73,146) | -2.51 (± 20.54) | 0.46 (± 21.69) | -1.03 (± 21.10) | |
| Change from BL at 3 Years (n=68,65,133) | -2.45 (± 20.42) | -3.59 (± 26.76) | -3.01 (± 23.64) | |

Notes:

[14] - n = participants with non-missing data at baseline and a given timepoint.

[15] - n = participants with non-missing data at baseline and a given timepoint.

[16] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Social Functioning Scale Score of the EORTC QLQ-C30

| | |
|-----------------|---|
| End point title | Change From Baseline Over Time in the Social Functioning Scale Score of the EORTC QLQ-C30 |
|-----------------|---|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 78 ^[17] | 80 ^[18] | 158 ^[19] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=78,80,158) | 77.99 (± 22.39) | 80.00 (± 21.28) | 79.01 (± 21.79) | |
| Change from BL at Cycle 3 Day 1 (n=77,80,157) | 5.41 (± 24.40) | 7.08 (± 20.84) | 6.26 (± 22.60) | |
| Change from BL at Cycle 6 Day 1 (n=75,79,154) | 6.44 (± 25.39) | 2.53 (± 20.16) | 4.44 (± 22.87) | |
| Change from BL at Cycle 15/Last Cycle(n=70,71,141) | 9.05 (± 23.86) | 6.57 (± 23.98) | 7.80 (± 23.87) | |
| Change from BL at 1.5 Years (n=71,74,145) | 12.21 (± 29.41) | 12.61 (± 18.05) | 12.41 (± 24.20) | |
| Change from BL at 2 Years (n=72,73,145) | 15.28 (± 25.29) | 12.10 (± 23.12) | 13.68 (± 24.19) | |
| Change from BL at 3 Years (n=67,65,132) | 11.94 (± 25.76) | 13.33 (± 23.24) | 12.63 (± 24.46) | |

Notes:

[17] - n = participants with non-missing data at baseline and a given timepoint.

[18] - n = participants with non-missing data at baseline and a given timepoint.

[19] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Fatigue Scale Score of the EORTC QLQ-C30

| | |
|-----------------|--|
| End point title | Change From Baseline Over Time in the Fatigue Scale Score of the EORTC QLQ-C30 |
|-----------------|--|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[20] | 80 ^[21] | 159 ^[22] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 24.47 (± 19.28) | 19.58 (± 18.31) | 22.01 (± 18.90) | |
| Change from BL at Cycle 3 Day 1 (n=79,80,159) | -0.14 (± 17.66) | 2.71 (± 14.92) | 1.29 (± 16.35) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | -3.22 (± 17.85) | 4.08 (± 19.91) | 0.50 (± 19.22) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | -3.44 (± 18.36) | -0.78 (± 24.22) | -2.11 (± 21.46) | |
| Change from BL at 1.5 Years (n=72,74,146) | -9.26 (± 20.43) | -6.31 (± 18.76) | -7.76 (± 19.59) | |
| Change from BL at 2 Years (n=73,73,146) | -6.54 (± 25.51) | -3.96 (± 23.52) | -5.25 (± 24.49) | |
| Change from BL at 3 Years (n=68,65,133) | -7.68 (± 21.66) | -3.08 (± 23.45) | -5.43 (± 22.58) | |

Notes:

[20] - n = participants with non-missing data at baseline and a given timepoint.

[21] - n = participants with non-missing data at baseline and a given timepoint.

[22] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Nausea and Vomiting Scale Score of the EORTC QLQ-C30

| | |
|-----------------|--|
| End point title | Change From Baseline Over Time in the Nausea and Vomiting Scale Score of the EORTC QLQ-C30 |
|-----------------|--|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[23] | 80 ^[24] | 159 ^[25] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 2.11 (± 7.24) | 3.33 (± 9.71) | 2.73 (± 8.57) | |
| Change from BL at Cycle 3 Day 1 (n=79,80,159) | 0.21 (± 9.80) | 1.46 (± 11.62) | 0.84 (± 10.74) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | 1.54 (± 11.92) | 0.00 (± 11.32) | 0.75 (± 11.61) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | 1.88 (± 12.13) | 0.47 (± 10.53) | 1.17 (± 11.34) | |
| Change from BL at 1.5 Years (n=72,74,146) | 0.46 (± 11.18) | -0.90 (± 11.67) | -0.23 (± 11.41) | |
| Change from BL at 2 Years (n=73,73,146) | -0.23 (± 11.28) | -1.14 (± 10.88) | -0.68 (± 11.05) | |
| Change from BL at 3 Years (n=68,65,133) | -1.23 (± 9.69) | -0.26 (± 11.97) | -0.75 (± 10.83) | |

Notes:

[23] - n = participants with non-missing data at baseline and a given timepoint.

[24] - n = participants with non-missing data at baseline and a given timepoint.

[25] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Pain Scale Score of the EORTC QLQ-C30

| | |
|-----------------|---|
| End point title | Change From Baseline Over Time in the Pain Scale Score of the EORTC QLQ-C30 |
|-----------------|---|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[26] | 80 ^[27] | 159 ^[28] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 17.72 (± 24.94) | 14.38 (± 19.26) | 16.04 (± 22.26) | |
| Change from BL at Cycle 3 Day 1 (n=79,80,159) | 0.00 (± 27.86) | 0.42 (± 22.02) | 0.21 (± 25.02) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | -2.41 (± 25.92) | 3.16 (± 20.34) | 0.43 (± 23.34) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | -2.82 (± 25.04) | 0.47 (± 26.72) | -1.17 (± 25.85) | |
| Change from BL at 1.5 Years (n=72,74,146) | -1.62 (± 33.47) | -0.90 (± 23.71) | -1.26 (± 28.84) | |
| Change from BL at 2 Years (n=73,73,146) | -1.83 (± 30.25) | -4.34 (± 23.25) | -3.08 (± 26.91) | |
| Change from BL at 3 Years (n=68,65,133) | -1.72 (± 26.88) | -2.56 (± 29.79) | -2.13 (± 28.23) | |

Notes:

[26] - n = participants with non-missing data at baseline and a given timepoint.

[27] - n = participants with non-missing data at baseline and a given timepoint.

[28] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Dyspnoea Scale Score of the EORTC QLQ-C30

| | |
|-----------------|---|
| End point title | Change From Baseline Over Time in the Dyspnoea Scale Score of the EORTC QLQ-C30 |
|-----------------|---|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[29] | 80 ^[30] | 159 ^[31] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 6.75 (± 15.45) | 5.00 (± 15.09) | 5.87 (± 15.25) | |
| Change from BL at Cycle 3 Day 1 (n=79,80,159) | -0.42 (± 14.61) | 1.67 (± 11.74) | 0.63 (± 13.24) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | 1.32 (± 15.81) | 4.64 (± 15.77) | 3.01 (± 15.83) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | 1.41 (± 19.05) | 2.35 (± 16.26) | 1.88 (± 17.65) | |
| Change from BL at 1.5 Years (n=72,74,146) | -0.46 (± 10.46) | 1.80 (± 16.45) | 0.68 (± 13.82) | |
| Change from BL at 2 Years (n=73,73,146) | 1.83 (± 16.56) | 1.83 (± 10.96) | 1.83 (± 14.00) | |
| Change from BL at 3 Years (n=68,65,133) | 1.47 (± 13.42) | 1.54 (± 14.94) | 1.50 (± 14.13) | |

Notes:

[29] - n = participants with non-missing data at baseline and a given timepoint.

[30] - n = participants with non-missing data at baseline and a given timepoint.

[31] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Insomnia Scale Score of the EORTC QLQ-C30

| | |
|-----------------|---|
| End point title | Change From Baseline Over Time in the Insomnia Scale Score of the EORTC QLQ-C30 |
|-----------------|---|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[32] | 80 ^[33] | 159 ^[34] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 21.94 (± 24.97) | 22.50 (± 25.86) | 22.22 (± 25.34) | |
| Change from BL at Cycle 3 Day 1 (n=79,80,159) | 2.95 (± 26.25) | -0.42 (± 27.81) | 1.26 (± 27.01) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | 5.26 (± 29.34) | -1.69 (± 30.15) | 1.72 (± 29.86) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | 3.76 (± 32.15) | -5.63 (± 30.85) | -0.94 (± 31.75) | |
| Change from BL at 1.5 Years (n=72,74,146) | 1.85 (± 30.07) | -2.25 (± 31.85) | -0.23 (± 30.95) | |
| Change from BL at 2 Years (n=73,73,146) | 6.85 (± 35.56) | -0.91 (± 31.90) | 2.97 (± 33.89) | |
| Change from BL at 3 Years (n=68,65,133) | 1.47 (± 33.79) | -1.54 (± 34.58) | 0.00 (± 34.08) | |

Notes:

[32] - n = participants with non-missing data at baseline and a given timepoint.

[33] - n = participants with non-missing data at baseline and a given timepoint.

[34] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Appetite Loss Scale Score of the EORTC QLQ-C30

| | |
|-----------------|--|
| End point title | Change From Baseline Over Time in the Appetite Loss Scale Score of the EORTC QLQ-C30 |
|-----------------|--|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[35] | 80 ^[36] | 159 ^[37] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 8.44 (± 14.59) | 11.67 (± 23.18) | 10.06 (± 19.40) | |
| Change from BL at Cycle 3 Day 1 (n=79,80,159) | 3.38 (± 23.02) | -2.92 (± 19.26) | 0.21 (± 21.38) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | 0.00 (± 18.86) | -1.69 (± 17.62) | -0.86 (± 18.20) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | -4.69 (± 17.18) | -6.10 (± 23.44) | -5.40 (± 20.49) | |
| Change from BL at 1.5 Years (n=72,74,146) | -4.63 (± 20.41) | -7.66 (± 19.54) | -6.16 (± 19.96) | |
| Change from BL at 2 Years (n=73,73,146) | -5.48 (± 15.73) | -3.20 (± 20.91) | -4.34 (± 18.47) | |
| Change from BL at 3 Years (n=68,65,133) | -5.39 (± 15.89) | -6.67 (± 22.97) | -6.02 (± 19.61) | |

Notes:

[35] - n = participants with non-missing data at baseline and a given timepoint.

[36] - n = participants with non-missing data at baseline and a given timepoint.

[37] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Constipation Scale Score of the EORTC QLQ-C30

| | |
|-----------------|---|
| End point title | Change From Baseline Over Time in the Constipation Scale Score of the EORTC QLQ-C30 |
|-----------------|---|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[38] | 80 ^[39] | 159 ^[40] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 8.44 (± 16.42) | 9.58 (± 21.99) | 9.01 (± 19.37) | |
| Change from BL at Cycle 3 Day 1 (n=79,80,159) | 0.00 (± 15.10) | -3.33 (± 18.06) | -1.68 (± 16.69) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | 0.88 (± 20.35) | -2.53 (± 18.31) | -0.86 (± 19.35) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | 0.00 (± 20.31) | -1.41 (± 22.14) | -0.70 (± 21.18) | |
| Change from BL at 1.5 Years (n=72,74,146) | 0.00 (± 17.69) | 0.45 (± 28.93) | 0.23 (± 23.97) | |
| Change from BL at 2 Years (n=73,73,146) | 5.94 (± 26.26) | -2.74 (± 27.08) | 1.60 (± 26.93) | |
| Change from BL at 3 Years (n=68,65,133) | 0.49 (± 20.36) | 2.56 (± 26.55) | 1.50 (± 23.52) | |

Notes:

[38] - n = participants with non-missing data at baseline and a given timepoint.

[39] - n = participants with non-missing data at baseline and a given timepoint.

[40] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Diarrhoea Scale Score of the EORTC QLQ-C30

| | |
|-----------------|--|
| End point title | Change From Baseline Over Time in the Diarrhoea Scale Score of the EORTC QLQ-C30 |
|-----------------|--|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[41] | 80 ^[42] | 159 ^[43] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 12.24 (± 22.76) | 8.75 (± 20.36) | 10.48 (± 21.59) | |
| Change from BL at Cycle 3 Day 1 (n=78,80,158) | 4.70 (± 25.04) | 9.58 (± 29.14) | 7.17 (± 27.22) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | 4.39 (± 23.31) | 5.49 (± 25.28) | 4.95 (± 24.26) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | 2.82 (± 25.66) | 2.35 (± 26.62) | 2.58 (± 26.06) | |
| Change from BL at 1.5 Years (n=72,74,146) | -8.33 (± 23.57) | -4.50 (± 20.88) | -6.39 (± 22.25) | |
| Change from BL at 2 Years (n=73,73,146) | -8.22 (± 26.52) | -5.48 (± 20.80) | -6.85 (± 23.79) | |
| Change from BL at 3 Years (n=68,65,133) | -9.80 (± 25.79) | -5.13 (± 21.43) | -7.52 (± 23.79) | |

Notes:

[41] - n = participants with non-missing data at baseline and a given timepoint.

[42] - n = participants with non-missing data at baseline and a given timepoint.

[43] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in the Financial Difficulties Scale Score of the EORTC QLQ-C30

| | |
|-----------------|---|
| End point title | Change From Baseline Over Time in the Financial Difficulties Scale Score of the EORTC QLQ-C30 |
|-----------------|---|

End point description:

The EORTC QLQ-C30 questionnaire consisted of 30 questions covering treatment-related symptoms, functioning, and GHS/HRQoL. Questions were answered by participants on a scale from 1 to 4 or 1 to 7. Raw scores were transformed to scale scores that ranged from 0 to 100 where a higher scale score indicating a higher response (i.e., on the functioning and GHS/QoL scales a higher score meant better functioning/QoL, whereas on the symptom scales a higher score meant greater [worse] symptoms). The EORTC QLQ-C30 data was scored according to the EORTC scoring manual (Fayers 2001). In the event of incomplete data, for all questionnaire subscales, if more than 50% of the constituent items are completed, a pro-rated score was to be computed consistent with the scoring manuals and published validation reports. For subscales with less than 50% of the items completed, the subscale was to be considered as missing.

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

End point timeframe:

Baseline (Day 1 of Cycle 1); Day 1 of Cycles 3, 6, and 15 (or last treatment cycle; each cycle is 21 days); 1.5, 2, and 3 years (up to 3 years)

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|---|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 79 ^[44] | 80 ^[45] | 159 ^[46] | |
| Units: Score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (BL): Value at Visit (n=79,80,159) | 23.63 (± 27.30) | 22.08 (± 28.04) | 22.85 (± 27.59) | |
| Change from BL at Cycle 3 Day 1 (n=78,80,158) | -2.99 (± 20.23) | -2.92 (± 24.42) | -2.95 (± 22.38) | |
| Change from BL at Cycle 6 Day 1 (n=76,79,155) | -4.39 (± 20.61) | 0.00 (± 24.46) | -2.15 (± 22.69) | |
| Change from BL at Cycle 15/Last Cycle(n=71,71,142) | -8.45 (± 25.02) | -8.45 (± 25.65) | -8.45 (± 25.24) | |
| Change from BL at 1.5 Years (n=72,74,146) | -13.89 (± 30.00) | -11.26 (± 26.62) | -12.56 (± 28.27) | |
| Change from BL at 2 Years (n=73,73,146) | -15.98 (± 27.84) | -12.79 (± 28.13) | -14.38 (± 27.93) | |
| Change from BL at 3 Years (n=68,65,133) | -14.71 (± 32.26) | -8.21 (± 29.48) | -11.53 (± 30.99) | |

Notes:

[44] - n = participants with non-missing data at baseline and a given timepoint.

[45] - n = participants with non-missing data at baseline and a given timepoint.

[46] - n = participants with non-missing data at baseline and a given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Summary for Assessment of Switching Between the FDC SC and IV Formulations: Number of Participants with at Least One Adverse Event During the Treatment Cross-Over Period by Treatment Arm and Treatment Received

| | |
|-----------------|--|
| End point title | Safety Summary for Assessment of Switching Between the FDC SC and IV Formulations: Number of Participants with at Least One Adverse Event During the Treatment Cross-Over Period by Treatment Arm and Treatment Received |
|-----------------|--|

End point description:

Investigators used the NCI CTCAE v4.0 grading scale for assessing adverse event (AE) severity; if not listed, AE severity was graded as follows: Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe or medically significant; Grade 4 = life-threatening; Grade 5 = death related to AE. Severity and seriousness are not synonymous and investigators independently assessed these criteria for each AE. Investigators also determined whether an AE was considered to be related to the study drug. Adverse events to monitor were defined based on known risks associated with the study drugs and included: hypersensitivity reactions, administration-related reactions (ARRs), cardiac dysfunction, diarrhea grade ≥3, rash/skin reactions, mucositis, interstitial lung disease (ILD), (febrile) neutropenia, pulmonary events that may occur as a result of an ARR, and pregnancy/neonatal related. Multiple occurrences of AEs were counted only once per participant. LVEF = left ventricular ejection fraction

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

End point timeframe:

From Day 1 of Cycle 1 to the end of Cycle 3 of Cross-Over Period; from Day 1 of Cycle 4 to the end of Cycle 6 of Cross-Over Period (1 cycle is 21 days)

| End point values | Arm A: Treatment With P+H IV (Cycles 1-3) | Arm A: Treatment With PH FDC SC (Cycles 4-6) | Arm B: Treatment With PH FDC SC (Cycles 1-3) | Arm B: Treatment With P+H IV (Cycles 4-6) |
|--|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 80 | 80 | 80 | 80 |
| Units: Participants | | | | |
| Any Adverse Event (AE) | 62 | 60 | 62 | 51 |
| AE with Fatal Outcome | 0 | 0 | 0 | 0 |
| Related AE with Fatal Outcome | 0 | 0 | 0 | 0 |
| Grade 3 to 5 AE | 1 | 1 | 3 | 4 |
| Related Grade 3 to 5 AE | 1 | 0 | 1 | 0 |
| Cardiac AE (Including LVEF Events) | 1 | 2 | 3 | 2 |
| Serious AE | 1 | 1 | 1 | 5 |
| Anaphylaxis and Hypersensitivity AE, All Grades | 0 | 2 | 1 | 0 |
| Anaphylaxis and Hypersensitivity AE, Grade ≥3 | 0 | 0 | 0 | 0 |
| Administration Related Reaction (ARR), All Grades | 7 | 14 | 24 | 2 |
| Administration Related Reaction (ARR), Grade ≥3 | 0 | 0 | 0 | 0 |
| Cardiac Dysfunction AE, All Grades | 2 | 1 | 3 | 3 |
| Cardiac Dysfunction AE, Grade ≥3 | 1 | 0 | 0 | 0 |
| Diarrhea Grade ≥3 | 0 | 0 | 1 | 0 |
| Rash/Skin Reactions | 0 | 0 | 0 | 0 |
| Mucositis | 0 | 0 | 0 | 0 |
| Pulmonary Events (ARR), All Grades | 18 | 8 | 4 | 8 |
| Pulmonary Events (ARR), Grade ≥3 | 0 | 0 | 1 | 0 |
| Pregnancy and Neonatal Related AEs, All Grades | 0 | 0 | 1 | 0 |
| Pregnancy and Neonatal Related AEs, Grade ≥3 | 0 | 0 | 0 | 0 |
| Interstitial Lung Disease (ILD) | 0 | 0 | 0 | 0 |
| Neutropenia/Febrile Neutropenia, All Grades | 4 | 1 | 2 | 3 |
| Neutropenia/Febrile Neutropenia, Grade ≥3 | 0 | 0 | 0 | 0 |
| Local Infusion Site Reaction | 1 | 0 | 0 | 0 |
| Systemic Infusion Site Reaction | 5 | 0 | 0 | 1 |
| Local Injection Site Reaction | 0 | 12 | 24 | 0 |
| Systemic Injection Site Reaction | 0 | 2 | 1 | 0 |
| AE Leading to Any Study Treatment Discontinuation | 0 | 1 | 0 | 0 |
| AE Leading to PH FDC SC Discontinuation | 0 | 1 | 0 | 0 |
| AE Leading to Pertuzumab IV Discontinuation | 0 | 0 | 0 | 0 |
| AE Leading to Trastuzumab IV Discontinuation | 0 | 0 | 0 | 0 |
| AE Leading to Any Study Trx Interrupt./Dose Reduc. | 1 | 0 | 2 | 3 |

Statistical analyses

Secondary: Safety Summary of the FDC SC and IV Formulations: Number of Participants with at Least One Adverse Event During the Treatment Cross-Over and Treatment Continuation Periods

| | |
|-----------------|---|
| End point title | Safety Summary of the FDC SC and IV Formulations: Number of Participants with at Least One Adverse Event During the Treatment Cross-Over and Treatment Continuation Periods |
|-----------------|---|

End point description:

Investigators used the NCI CTCAE v4.0 grading scale for assessing adverse event (AE) severity; if not listed, AE severity was graded as follows: Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe or medically significant; Grade 4 = life-threatening; Grade 5 = death related to AE. Severity and seriousness are not synonymous and investigators independently assessed these criteria for each AE. Investigators also determined whether an AE was considered to be related to the study drug. Adverse events to monitor were defined based on known risks associated with the study drugs and included: hypersensitivity reactions, administration-related reactions (ARRs), cardiac dysfunction, diarrhea grade ≥ 3 , rash/skin reactions, mucositis, interstitial lung disease (ILD), (febrile) neutropenia, pulmonary events that may occur as a result of an ARR, and pregnancy/neonatal related. Multiple occurrences of AEs were counted only once per participant. LVEF = left ventricular ejection fraction

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

End point timeframe:

From Day 1 of Cycle 1 to end of Cycle 6 of the Treatment Cross-Over Period; from Day 1 of Cycle 7 up to the completion of 18 cycles of neo/adjuvant anti-HER2 treatment in the Treatment Continuation Period (1 cycle is 21 days)

| End point values | P+H IV: Treatment Cross-Over Period | PH FDC SC: Treatment Cross-Over Period | P+H IV: Treatment Continuation Period | PH FDC SC: Treatment Continuation Period |
|---|--|---|--|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 160 | 160 | 21 | 138 |
| Units: Participants | | | | |
| Any Adverse Event (AE) | 113 | 122 | 14 | 92 |
| AE with Fatal Outcome | 0 | 0 | 0 | 0 |
| Related AE with Fatal Outcome | 0 | 0 | 0 | 0 |
| Grade 3 to 5 AE | 5 | 4 | 2 | 7 |
| Related Grade 3 to 5 AE | 1 | 1 | 0 | 0 |
| Cardiac AE (Including LVEF Events) | 3 | 5 | 1 | 1 |
| Serious AE | 6 | 2 | 0 | 4 |
| Anaphylaxis and Hypersensitivity AE, All Grades | 0 | 3 | 0 | 2 |
| Anaphylaxis and Hypersensitivity AE, Grade ≥ 3 | 0 | 0 | 0 | 0 |
| Administration Related Reaction (ARR), All Grades | 9 | 38 | 1 | 16 |
| Administration Related Reaction (ARR), Grade ≥ 3 | 0 | 0 | 0 | 0 |
| Cardiac Dysfunction AE, All Grades | 5 | 4 | 1 | 2 |
| Cardiac Dysfunction AE, Grade ≥ 3 | 1 | 0 | 0 | 0 |
| Diarrhea Grade ≥ 3 | 0 | 1 | 0 | 0 |
| Rash/Skin Reactions | 0 | 0 | 0 | 0 |
| Mucositis | 0 | 0 | 0 | 0 |
| Pulmonary Events (ARR), All Grades | 26 | 12 | 5 | 13 |
| Pulmonary Events (ARR), Grade ≥ 3 | 0 | 1 | 0 | 0 |

| | | | | |
|--|---|----|---|----|
| Pregnancy and Neonatal Related AEs, All Grades | 0 | 1 | 0 | 0 |
| Pregnancy and Neonatal Related AEs, Grade ≥ 3 | 0 | 0 | 0 | 0 |
| Interstitial Lung Disease (ILD), All Grades | 0 | 0 | 0 | 1 |
| Interstitial Lung Disease (ILD), Grade ≥ 3 | 0 | 0 | 0 | 0 |
| Neutropenia/Febrile Neutropenia, All Grades | 7 | 3 | 1 | 5 |
| Neutropenia/Febrile Neutropenia, Grade ≥ 3 | 0 | 0 | 0 | 1 |
| Local Infusion Site Reaction | 1 | 0 | 0 | 0 |
| Systemic Infusion Site Reaction | 6 | 0 | 1 | 0 |
| Local Injection Site Reaction | 0 | 36 | 0 | 13 |
| Systemic Injection Site Reaction | 0 | 3 | 0 | 2 |
| AE Leading to Any Study Treatment Discontinuation | 0 | 1 | 1 | 0 |
| AE Leading to PH FDC SC Discontinuation | 0 | 1 | 0 | 0 |
| AE Leading to Pertuzumab IV Discontinuation | 0 | 0 | 1 | 0 |
| AE Leading to Trastuzumab IV Discontinuation | 0 | 0 | 1 | 0 |
| AE Leading to Any Study Trx Interrupt./Dose Reduc. | 4 | 2 | 1 | 8 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with at Least One Event of Ejection Fraction Decreased with the FDC SC and IV Formulations During the Treatment Cross-Over and Treatment Continuation Periods

| | |
|-----------------|--|
| End point title | Number of Participants with at Least One Event of Ejection Fraction Decreased with the FDC SC and IV Formulations During the Treatment Cross-Over and Treatment Continuation Periods |
|-----------------|--|

End point description:

Left ventricular ejection fraction (LVEF) is the measurement of how much blood is being pumped out of the left ventricle of the heart (the main pumping chamber) with each contraction. All participants who enrolled in this study must have had a baseline LVEF $\geq 55\%$. Verbatim description of adverse events was mapped to Medical Dictionary for Regulatory Activities (MedDRA) version 22.1. The MedDRA preferred term of 'ejection fraction decreased' is defined as an LVEF decrease of at least 10 percentage points from baseline and to below 50%.

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

End point timeframe:

Baseline; Day 1 of Cycles 4, 7, and 11 (each cycle is 21 days); End of Treatment and Follow-Up visits (up to 3 years)

| End point values | P+H IV: Treatment Cross-Over Period | PH FDC SC: Treatment Cross-Over Period | P+H IV: Treatment Continuation Period | PH FDC SC: Treatment Continuation Period |
|-----------------------------|--|---|--|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 160 | 160 | 21 | 138 |
| Units: Participants | 3 | 4 | 1 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with at Least One Event of Heart Failure with the FDC SC and IV Formulations During the Treatment Cross-Over and Treatment Continuation Periods

| | |
|-----------------|--|
| End point title | Number of Participants with at Least One Event of Heart Failure with the FDC SC and IV Formulations During the Treatment Cross-Over and Treatment Continuation Periods |
|-----------------|--|

End point description:

Heart failure is defined as a disorder characterized by the inability of the heart to pump blood at an adequate volume to meet tissue metabolic requirements, or, the ability to do only at an elevation in the filling pressure. Any adverse event of symptomatic left ventricular systolic dysfunction (LVSD; also referred to as heart failure) occurring during the study was to be reported as a serious adverse event.

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

End point timeframe:

From Day 1 of Cycle 1 to end of Cycle 6 of the Treatment Cross-Over Period; from Day 1 of Cycle 7 up to the completion of 18 cycles of neo/adjuvant anti-HER2 treatment in the Treatment Continuation Period (1 cycle is 21 days)

| End point values | P+H IV: Treatment Cross-Over Period | PH FDC SC: Treatment Cross-Over Period | P+H IV: Treatment Continuation Period | PH FDC SC: Treatment Continuation Period |
|-----------------------------|--|---|--|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 160 | 160 | 21 | 138 |
| Units: Participants | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Targeted Vital Signs Outside the Normal Limits Among Those Without an Abnormality at Baseline During the Treatment Cross-Over and Treatment Continuation Periods

| | |
|-----------------|--|
| End point title | Number of Participants with Targeted Vital Signs Outside the Normal Limits Among Those Without an Abnormality at Baseline During the Treatment Cross-Over and Treatment Continuation Periods |
|-----------------|--|

End point description:

The number of participants at any post-baseline timepoint with abnormal readings outside the normal range for vital signs of diastolic and systolic blood pressure (BP), pulse rate, respiratory rate, and body temperature were summarized according the specified direction of the abnormal reading (high or low). In this analysis, participants are grouped by study arm and treatment received during the Cross-Over Period, and only by treatment received during the Continuation Period. The number analyzed (denominator) in the results table represents participants without the specified abnormal vital sign at baseline.

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

End point timeframe:

Pre-dose at Day 1 of Cycles 1 (baseline), 4, and 7, and end of treatment (up to 18 cycles; 1 cycle is 21 days)

| End point values | Arm A: Treatment With P+H IV (Cycles 1-3) | Arm A: Treatment With PH FDC SC (Cycles 4-6) | Arm B: Treatment With PH FDC SC (Cycles 1-3) | Arm B: Treatment With P+H IV (Cycles 4-6) |
|---|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 80 | 80 | 80 | 80 |
| Units: Participants | | | | |
| Diastolic BP - Low (n=80,77,80,80,20,137) | 0 | 0 | 0 | 0 |
| Diastolic BP - High (n=80,77,78,78,20,135) | 2 | 2 | 0 | 0 |
| Systolic BP - Low (n=80,77,80,80,20,137) | 0 | 0 | 0 | 0 |
| Systolic BP - High (n=77,74,75,75,20,129) | 8 | 7 | 3 | 3 |
| Pulse Rate - Low (n=80,77,80,80,20,137) | 0 | 0 | 0 | 0 |
| Pulse Rate - High (n=75,72,75,75,19,128) | 1 | 0 | 0 | 1 |
| Respiratory Rate - Low (n=80,77,80,79,20,137) | 0 | 0 | 0 | 0 |
| Respiratory Rate - High (n=80,77,79,78,20,136) | 1 | 0 | 2 | 2 |
| Temperature - Low (n=54,51,39,39,12,80) | 22 | 17 | 10 | 13 |
| Temperature - High (n=80,77,80,80,21,137) | 0 | 0 | 1 | 0 |

| End point values | P+H IV: Treatment Continuation Period | PH FDC SC: Treatment Continuation Period | | |
|---|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 21 | 138 | | |
| Units: Participants | | | | |
| Diastolic BP - Low (n=80,77,80,80,20,137) | 0 | 0 | | |
| Diastolic BP - High (n=80,77,78,78,20,135) | 0 | 3 | | |
| Systolic BP - Low (n=80,77,80,80,20,137) | 0 | 0 | | |

| | | | | |
|---|---|----|--|--|
| Systolic BP - High (n=77,74,75,75,20,129) | 1 | 12 | | |
| Pulse Rate - Low (n=80,77,80,80,20,137) | 0 | 0 | | |
| Pulse Rate - High (n=75,72,75,75,19,128) | 1 | 1 | | |
| Respiratory Rate - Low (n=80,77,80,79,20,137) | 0 | 0 | | |
| Respiratory Rate - High (n=80,77,79,78,20,136) | 0 | 4 | | |
| Temperature - Low (n=54,51,39,39,12,80) | 4 | 34 | | |
| Temperature - High (n=80,77,80,80,21,137) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Chemistry and Hematology Laboratory Test Result Shifts from NCI-CTCAE Grade 0–2 at Baseline to Grade 3–4 Post-Baseline During the Treatment Cross-Over and Treatment Continuation Periods

| | |
|-----------------|---|
| End point title | Number of Participants with Chemistry and Hematology Laboratory Test Result Shifts from NCI-CTCAE Grade 0–2 at Baseline to Grade 3–4 Post-Baseline During the Treatment Cross-Over and Treatment Continuation Periods |
|-----------------|---|

End point description:

Laboratory data for targeted chemistry and hematology parameters were classified according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0 (NCI CTCAE v4.0); Grade 0 is normal and Grades 1 to 4 represent worsening levels of the laboratory parameter outside of the normal range in the specified direction of the abnormality (e.g., high is an increase, low is a decrease). The results table presents the shifts in the number of participants with NCI-CTCAE Grade 0–2 at baseline to Grade 3–4 post-baseline for the targeted parameters according to the specified direction of the abnormality outside of the normal range (high or low). Participants with missing baseline values were counted as Grade 0–2 at baseline. SGOT/AST = aspartate aminotransferase; SGPT/ALT = alanine aminotransferase

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

End point timeframe:

Pre-dose at Day 1 of Cycles 1 (baseline), 4, 7, 11, 15, and end of treatment (up to 18 cycles; 1 cycle is 21 days)

| End point values | Arm A: Treatment With P+H IV (Cycles 1–3) | Arm A: Treatment With PH FDC SC (Cycles 4–6) | Arm B: Treatment With PH FDC SC (Cycles 1–3) | Arm B: Treatment With P+H IV (Cycles 4–6) |
|---|--|---|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 80 | 80 | 80 | 80 |
| Units: Participants | | | | |
| Alkaline Phosphatase - High (n=78,79,78,78,21,136) | 0 | 0 | 0 | 0 |
| SGPT/ALT - High (n=78,79,78,79,21,136) | 0 | 0 | 0 | 0 |
| SGOT/AST - High (n=77,78,79,79,21,136) | 0 | 0 | 0 | 0 |

| | | | | |
|---|---|---|---|---|
| Creatinine - High (n=80,78,79,77,21,136) | 0 | 0 | 0 | 0 |
| Bilirubin, Total - High (n=76,79,79,79,21,136) | 0 | 0 | 0 | 0 |
| Hemoglobin - Low (n=80,78,79,80,21,136) | 0 | 0 | 0 | 0 |
| Hemoglobin - High (n=80,78,79,80,21,136) | 0 | 0 | 0 | 0 |
| Neutrophils, Total,Abs - Low(n=80,78,79,80,21,136) | 0 | 0 | 0 | 0 |
| Platelet - Low (n=80,78,79,80,21,136) | 0 | 0 | 0 | 0 |
| Total Leukocyte Count - Low (n=80,78,79,80,21,136) | 0 | 0 | 0 | 0 |
| Total Leukocyte Count - High(n=80,78,79,80,21,136) | 0 | 0 | 0 | 0 |

| End point values | P+H IV: Treatment Continuation Period | PH FDC SC: Treatment Continuation Period | | |
|---|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 21 | 138 | | |
| Units: Participants | | | | |
| Alkaline Phosphatase - High (n=78,79,78,78,21,136) | 0 | 0 | | |
| SGPT/ALT - High (n=78,79,78,79,21,136) | 0 | 0 | | |
| SGOT/AST - High (n=77,78,79,79,21,136) | 0 | 0 | | |
| Creatinine - High (n=80,78,79,77,21,136) | 0 | 0 | | |
| Bilirubin, Total - High (n=76,79,79,79,21,136) | 0 | 0 | | |
| Hemoglobin - Low (n=80,78,79,80,21,136) | 0 | 0 | | |
| Hemoglobin - High (n=80,78,79,80,21,136) | 0 | 0 | | |
| Neutrophils, Total,Abs - Low(n=80,78,79,80,21,136) | 0 | 2 | | |
| Platelet - Low (n=80,78,79,80,21,136) | 0 | 0 | | |
| Total Leukocyte Count - Low (n=80,78,79,80,21,136) | 0 | 1 | | |
| Total Leukocyte Count - High(n=80,78,79,80,21,136) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of the Percentage of Participants Who Were Event-Free for Overall Survival, Overall and by Treatment Sequence

| | |
|-----------------|---|
| End point title | Kaplan-Meier Estimate of the Percentage of Participants Who Were Event-Free for Overall Survival, Overall and by Treatment Sequence |
|-----------------|---|

End point description:

Overall survival is defined as the time from randomization to death due to any cause. Participants who were not reported as having died at the time of analysis were censored at the date when they were last known to be alive. Participants who did not have post-baseline information were censored at the date of randomization +1 day. Kaplan-Meier methodology was used to estimate the percentage of participants who were alive (event-free) at 12, 24, and 36 months.

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

End point timeframe:

At 12, 24, and 36 months

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|-----------------------------------|---------------------------------------|---------------------------------------|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 ^[47] | 80 ^[48] | 160 ^[49] | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 12 Months (n= 79, 78, 157) | 100.00 (100.00 to 100.00) | 100.00 (100.00 to 100.00) | 100.00 (100.00 to 100.00) | |
| 24 Months (n= 76, 75, 151) | 98.73 (96.27 to 100.00) | 100.00 (100.00 to 100.00) | 99.36 (98.12 to 100.00) | |
| 36 Months (n= 44, 53, 97) | 97.44 (93.93 to 100.00) | 100.00 (100.00 to 100.00) | 98.71 (96.92 to 100.00) | |

Notes:

[47] - n = number remaining at risk for an event

[48] - n = number remaining at risk for an event

[49] - n = number remaining at risk for an event

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with an Event for Overall Survival, Overall and by Treatment Sequence

| | |
|-----------------|--|
| End point title | Number of Participants with an Event for Overall Survival, Overall and by Treatment Sequence |
|-----------------|--|

End point description:

Overall survival (OS) is defined as the time from randomization to death due to any cause. The number of participants who had an OS event (i.e., died) while on study is reported.

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

End point timeframe:

Up to 3 years, 10 months

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|-----------------------------|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 | 80 | 160 | |
| Units: Participants | 2 | 0 | 2 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of the Percentage of Participants Who Were Event-Free for Invasive Disease-Free Survival Including Second Primary Non-Breast Cancer, Overall and by Treatment Sequence

| | |
|-----------------|--|
| End point title | Kaplan-Meier Estimate of the Percentage of Participants Who Were Event-Free for Invasive Disease-Free Survival Including Second Primary Non-Breast Cancer, Overall and by Treatment Sequence |
|-----------------|--|

End point description:

Invasive Disease-Free Survival is defined as the time from randomization to the first occurrence of one of the following events: ipsilateral invasive breast tumour recurrence, ipsilateral local-regional invasive breast cancer recurrence, distant recurrence, contralateral invasive breast cancer, and death from any cause. Second primary non-breast invasive cancer (with the exception of non-melanoma skin cancers and in situ carcinoma of any site) was included as an event. Participants who had not experienced invasive disease at the time of analysis were censored: i) at the time of the last clinical breast examination if they had post-baseline clinical breast examination; ii) on the date of randomization +1 day if no post-baseline clinical breast examination. Kaplan-Meier methodology was used to estimate the percentage of participants who were event-free at 12, 24, and 36 months.

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

End point timeframe:

At 12, 24, and 36 months

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|-----------------------------------|---------------------------------------|---------------------------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 ^[50] | 80 ^[51] | 160 ^[52] | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 12 Months (n= 75, 78, 153) | 94.94 (90.10 to 99.77) | 100.00 (100.00 to 100.00) | 97.46 (95.00 to 99.92) | |
| 24 Months (n= 71, 72, 143) | 92.37 (86.50 to 98.24) | 97.38 (93.80 to 100.00) | 94.87 (91.40 to 98.33) | |
| 36 Months (n= 36, 46, 82) | 91.05 (84.72 to 97.38) | 96.03 (91.63 to 100.00) | 93.53 (89.65 to 97.41) | |

Notes:

[50] - n = number remaining at risk for an event

[51] - n = number remaining at risk for an event

[52] - n = number remaining at risk for an event

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with an Event for Invasive Disease-Free Survival Including Second Primary Non-Breast Cancer, Overall and by Treatment Sequence

| | |
|-----------------|---|
| End point title | Number of Participants with an Event for Invasive Disease-Free Survival Including Second Primary Non-Breast Cancer, Overall and by Treatment Sequence |
|-----------------|---|

End point description:

Invasive Disease-Free Survival is defined as the time from randomization to the first occurrence of one of the following events: ipsilateral invasive breast tumour recurrence, ipsilateral local-regional invasive breast cancer recurrence, distant recurrence, contralateral invasive breast cancer, and death from any cause. Second primary non-breast invasive cancer (with the exception of non-melanoma skin cancers and in situ carcinoma of any site) was included as an event.

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

End point timeframe:

Up to 3 years, 10 months

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|-----------------------------|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 | 80 | 160 | |
| Units: Participants | 7 | 5 | 12 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of the Percentage of Participants Who Were Event-Free for Invasive Disease-Free Survival, Overall and by Treatment Sequence

| | |
|-----------------|---|
| End point title | Kaplan-Meier Estimate of the Percentage of Participants Who Were Event-Free for Invasive Disease-Free Survival, Overall and by Treatment Sequence |
|-----------------|---|

End point description:

Invasive Disease-Free Survival is defined as the time from randomization to the first occurrence of one of the following events: ipsilateral invasive breast tumour recurrence, ipsilateral local-regional invasive breast cancer recurrence, distant recurrence, contralateral invasive breast cancer, and death from any cause. Ipsilateral or contralateral in situ disease and second primary non-breast cancers (including in situ carcinomas and non-melanoma skin cancers) were not counted as recurrence. Participants who had not experienced invasive disease at the time of analysis were censored: i) at the time of the last clinical breast examination if they had post-baseline clinical breast examination; ii) on the date of randomization +1 day if no post-baseline clinical breast examination. Kaplan-Meier methodology was used to estimate the percentage of participants who were event-free at 12, 24, and 36 months.

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

End point timeframe:

At 12, 24, and 36 months

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|-----------------------------------|---------------------------------------|---------------------------------------|----------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 ^[53] | 80 ^[54] | 160 ^[55] | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 12 Months (n= 76, 78, 154) | 96.20 (91.99 to 100.00) | 100.00 (100.00 to 100.00) | 98.10 (95.96 to 100.00) | |
| 24 Months (n= 72, 72, 144) | 93.64 (88.24 to 99.03) | 97.38 (93.80 to 100.00) | 95.51 (92.25 to 98.76) | |
| 36 Months (n= 36, 46, 82) | 92.32 (86.41 to 98.23) | 96.03 (91.63 to 100.00) | 94.17 (90.47 to 97.87) | |

Notes:

[53] - n = number remaining at risk for an event

[54] - n = number remaining at risk for an event

[55] - n = number remaining at risk for an event

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with an Event for Invasive Disease-Free Survival, Overall and by Treatment Sequence

| | |
|-----------------|--|
| End point title | Number of Participants with an Event for Invasive Disease-Free Survival, Overall and by Treatment Sequence |
|-----------------|--|

End point description:

Invasive Disease-Free Survival is defined as the time from randomization to the first occurrence of one of the following events: ipsilateral invasive breast tumour recurrence, ipsilateral local-regional invasive breast cancer recurrence, distant recurrence, contralateral invasive breast cancer, and death from any cause. Ipsilateral or contralateral in situ disease and second primary non-breast cancers (including in situ carcinomas and non-melanoma skin cancers) were not counted as recurrence.

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

End point timeframe:

Up to 3 years, 10 months

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|-----------------------------|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 | 80 | 160 | |
| Units: Participants | 6 | 5 | 11 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with an Event for Distant Disease-Free Survival, Overall and by Treatment Sequence

| | |
|-----------------|---|
| End point title | Number of Participants with an Event for Distant Disease-Free |
|-----------------|---|

End point description:

Distant disease-free survival (DDFS) is defined as the time from randomization to the date of distant breast cancer recurrence (i.e., evidence of breast cancer in any anatomic site other than for ipsilateral [loco-regional] invasive breast cancer recurrence that has either been histologically confirmed or clinically diagnosed as recurrent invasive breast cancer).

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

End point timeframe:

Up to 3 years, 10 months

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|-----------------------------|---------------------------------------|---------------------------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 | 80 | 160 | |
| Units: Participants | 5 | 4 | 9 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan-Meier Estimate of the Percentage of Participants Who Were Event-Free for Distant Disease-Free Survival, Overall and by Treatment Sequence

| | |
|-----------------|--|
| End point title | Kaplan-Meier Estimate of the Percentage of Participants Who Were Event-Free for Distant Disease-Free Survival, Overall and by Treatment Sequence |
|-----------------|--|

End point description:

Distant disease-free survival (DDFS) is defined as the time from randomization to the date of distant breast cancer recurrence (i.e., evidence of breast cancer in any anatomic site other than for ipsilateral [loco-regional] invasive breast cancer recurrence that has either been histologically confirmed or clinically diagnosed as recurrent invasive breast cancer). Participants who had not experienced invasive disease at the time of analysis were censored: i) at the time of the last clinical breast examination if they had post-baseline clinical breast examination; ii) on the date of randomization +1 day if no post-baseline clinical breast examination. Kaplan-Meier methodology was used to estimate the percentage of participants who were event-free at 12, 24, and 36 months.

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

End point timeframe:

Up to 3 years

| End point values | A: P+H IV Followed by PH FDC SC | B: PH FDC SC Followed by P+H IV | All Participants | |
|-----------------------------------|---------------------------------------|---------------------------------------|-------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 80 ^[56] | 80 ^[57] | 160 ^[58] | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| 12 Months (n= 77, 78, 155) | 97.47 (94.00 to 100.00) | 100.00 (100.00 to 100.00) | 98.73 (96.98 to 100.00) | |

| | | | | |
|----------------------------|------------------------|-------------------------|------------------------|--|
| 24 Months (n= 73, 72, 145) | 94.90 (90.04 to 99.77) | 97.38 (93.80 to 100.00) | 96.14 (93.11 to 99.17) | |
| 36 Months (n= 37, 46, 83) | 93.58 (88.14 to 99.03) | 96.03 (91.63 to 100.00) | 94.80 (91.30 to 98.31) | |

Notes:

[56] - n = number remaining at risk for an event

[57] - n = number remaining at risk for an event

[58] - n = number remaining at risk for an event

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Cross-Over Period: 6 total cycles (3 cycles each of P+H IV and PH FDC SC); Continuation Period: 8 cycles of P+H IV or PH FDC SC (1 cycle is 21 days). Includes AEs with onset from first dose through 28 days after last dose of study treatment.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Pertuzumab IV and Trastuzumab IV: Cross-Over Period |
|-----------------------|---|

Reporting group description:

This safety analysis population includes all participants from arms A and B who received up to 3 cycles (1 cycle = 21 days) of treatment with pertuzumab IV and trastuzumab IV during the Treatment Cross-Over Period of the study.

| | |
|-----------------------|--|
| Reporting group title | Pertuzumab and Trastuzumab FDC SC: Cross-Over Period |
|-----------------------|--|

Reporting group description:

This safety analysis population includes all participants from arms A and B who received up to 3 cycles (1 cycle = 21 days) of treatment with the pertuzumab and trastuzumab fixed dose combination administered subcutaneously (FDC SC) during the Treatment Cross-Over Period of the study.

| | |
|-----------------------|------------------|
| Reporting group title | All Participants |
|-----------------------|------------------|

Reporting group description:

This safety analysis population includes all participants from Arms A and B who received at least one dose of treatment with pertuzumab IV and trastuzumab IV (P+H IV) and/or the pertuzumab and trastuzumab fixed-dose combination for subcutaneous administration (PH FDC SC) across any of the treatment periods during the study through 28 days after the last dose of study treatment. In addition, the number of deaths reported includes the study's survival follow-up period beyond 28 days after the last dose of study treatment (≥ 3 years after randomization).

| | |
|-----------------------|--|
| Reporting group title | Pertuzumab and Trastuzumab FDC SC: Continuation Period |
|-----------------------|--|

Reporting group description:

This safety analysis population includes all participants from arms A and B who, following completion of the Treatment Cross-Over Period, chose to receive the pertuzumab and trastuzumab fixed dose combination administered subcutaneously (FDC SC) during the Treatment Continuation Period for the remaining anti-HER2 treatment cycles (18 planned cycles in total, including pre-study neoadjuvant treatment).

| | |
|-----------------------|---|
| Reporting group title | Pertuzumab IV and Trastuzumab IV: Continuation Period |
|-----------------------|---|

Reporting group description:

This safety analysis population includes all participants from arms A and B who, following completion of the Treatment Cross-Over Period, chose to receive pertuzumab IV and trastuzumab IV during the Treatment Continuation Period for the remaining anti-HER2 treatment cycles (18 planned cycles in total, including pre-study neoadjuvant treatment).

| Serious adverse events | Pertuzumab IV and Trastuzumab IV: Cross-Over Period | Pertuzumab and Trastuzumab FDC SC: Cross-Over Period | All Participants |
|---|---|--|------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 160 (3.75%) | 2 / 160 (1.25%) | 11 / 160 (6.88%) |
| number of deaths (all causes) | 0 | 0 | 2 |
| number of deaths resulting from adverse events | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| Investigations | | | |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 1 / 160 (0.63%) | 2 / 160 (1.25%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 1 / 160 (0.63%) | 1 / 160 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 160 (0.00%) | 2 / 160 (1.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 160 (0.00%) | 2 / 160 (1.25%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Breast cellulitis | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 160 (0.00%) | 1 / 160 (0.63%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopulmonary aspergillosis | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 160 (0.00%) | 1 / 160 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 160 (0.00%) | 1 / 160 (0.63%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 160 (0.63%) | 0 / 160 (0.00%) | 1 / 160 (0.63%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 160 (0.00%) | 1 / 160 (0.63%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Pertuzumab and Trastuzumab FDC SC: Continuation Period | Pertuzumab IV and Trastuzumab IV: Continuation Period | |
|---|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 4 / 138 (2.90%) | 0 / 21 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 0 / 138 (0.00%) | 0 / 21 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 138 (0.00%) | 0 / 21 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Device related infection | | | |
| subjects affected / exposed | 1 / 138 (0.72%) | 0 / 21 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Erysipelas | | | |
| subjects affected / exposed | 2 / 138 (1.45%) | 0 / 21 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Breast cellulitis | | | |

| | | | |
|---|-----------------|----------------|--|
| subjects affected / exposed | 0 / 138 (0.00%) | 0 / 21 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopulmonary aspergillosis | | | |
| subjects affected / exposed | 1 / 138 (0.72%) | 0 / 21 (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 | 0 / 138 (0.00%) | 0 / 21 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 138 (0.00%) | 0 / 21 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 138 (0.72%) | 0 / 21 (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 | Pertuzumab IV and Trastuzumab IV: Cross-Over Period | Pertuzumab and Trastuzumab FDC SC: Cross-Over Period | All Participants |
|---|---|--|--------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 62 / 160 (38.75%) | 84 / 160 (52.50%) | 125 / 160 (78.13%) |
| Injury, poisoning and procedural complications | | | |
| Radiation skin injury | | | |
| subjects affected / exposed | 27 / 160 (16.88%) | 17 / 160 (10.63%) | 44 / 160 (27.50%) |
| occurrences (all) | 29 | 17 | 47 |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 6 / 160 (3.75%) | 9 / 160 (5.63%) | 16 / 160 (10.00%) |
| occurrences (all) | 6 | 10 | 19 |

| | | | |
|--|-------------------|-------------------|-------------------|
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 3 / 160 (1.88%) | 5 / 160 (3.13%) | 10 / 160 (6.25%) |
| occurrences (all) | 3 | 6 | 13 |
| General disorders and administration site conditions | | | |
| Injection site reaction | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 36 / 160 (22.50%) | 44 / 160 (27.50%) |
| occurrences (all) | 0 | 50 | 78 |
| Fatigue | | | |
| subjects affected / exposed | 8 / 160 (5.00%) | 9 / 160 (5.63%) | 19 / 160 (11.88%) |
| occurrences (all) | 8 | 10 | 29 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 17 / 160 (10.63%) | 15 / 160 (9.38%) | 37 / 160 (23.13%) |
| occurrences (all) | 20 | 19 | 66 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 2 / 160 (1.25%) | 3 / 160 (1.88%) | 10 / 160 (6.25%) |
| occurrences (all) | 3 | 3 | 12 |
| Pruritus | | | |
| subjects affected / exposed | 7 / 160 (4.38%) | 3 / 160 (1.88%) | 14 / 160 (8.75%) |
| occurrences (all) | 8 | 3 | 18 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 6 / 160 (3.75%) | 8 / 160 (5.00%) | 23 / 160 (14.38%) |
| occurrences (all) | 8 | 9 | 26 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 160 (0.00%) | 0 / 160 (0.00%) | 2 / 160 (1.25%) |
| occurrences (all) | 0 | 0 | 2 |
| Myalgia | | | |
| subjects affected / exposed | 6 / 160 (3.75%) | 3 / 160 (1.88%) | 12 / 160 (7.50%) |
| occurrences (all) | 6 | 3 | 12 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 160 (0.63%) | 4 / 160 (2.50%) | 9 / 160 (5.63%) |
| occurrences (all) | 1 | 5 | 13 |

| | | | |
|-----------------------------------|----------------|-------------------|--|
| Non-serious adverse events | Pertuzumab and | Pertuzumab IV and | |
|-----------------------------------|----------------|-------------------|--|

| | Trastuzumab FDC SC: Continuation Period | Trastuzumab IV: Continuation Period | |
|--|--|---|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 47 / 138 (34.06%) | 10 / 21 (47.62%) | |
| Injury, poisoning and procedural complications Radiation skin injury subjects affected / exposed occurrences (all) | 1 / 138 (0.72%) 1 | 0 / 21 (0.00%) 0 | |
| Vascular disorders Hot flush subjects affected / exposed occurrences (all) | 3 / 138 (2.17%) 3 | 0 / 21 (0.00%) 0 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 1 / 138 (0.72%) 1 | 2 / 21 (9.52%) 3 | |
| General disorders and administration site conditions Injection site reaction subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) | 13 / 138 (9.42%) 28 7 / 138 (5.07%) 8 | 0 / 21 (0.00%) 0 1 / 21 (4.76%) 3 | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 15 / 138 (10.87%) 23 | 4 / 21 (19.05%) 4 | |
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) | 2 / 138 (1.45%) 3 7 / 138 (5.07%) 7 | 3 / 21 (14.29%) 3 0 / 21 (0.00%) 0 | |
| Musculoskeletal and connective tissue disorders Arthralgia | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 6 / 138 (4.35%) | 3 / 21 (14.29%) | |
| occurrences (all) | 6 | 3 | |
| Bone pain | | | |
| subjects affected / exposed | 0 / 138 (0.00%) | 2 / 21 (9.52%) | |
| occurrences (all) | 0 | 2 | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 138 (0.72%) | 2 / 21 (9.52%) | |
| occurrences (all) | 1 | 2 | |
| Pain in extremity | | | |
| subjects affected / exposed | 4 / 138 (2.90%) | 2 / 21 (9.52%) | |
| occurrences (all) | 5 | 2 | |

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