ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
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Study Identification

Unique Protocol ID:	MO22982
Brief Title:	Participant Preference of Subcutaneous (SC) Versus Intravenous (IV) Herceptin (Trastuzumab) in Human Epidermal Growth Factor Receptor (HER) 2-Positive Early Breast Cancer (PrefHER)
Official Title:	A Randomized, Multi-Center Cross-Over Study to Evaluate Patient Preference and Health Care Professional (HCP) Satisfaction With Subcutaneous (SC) Administration of Trastuzumab in HER2-Positive Early Breast Cancer (EBC)
Secondary IDs:	2010-024099-25 [EudraCT Number]

Study Status

Record Verification:	January 2017
Overall Status:	Completed
Study Start:	October 2011 []
Primary Completion:	May 2013 [Actual]
Study Completion:	December 2015 [Actual]

Sponsor/Collaborators

Sponsor:	Hoffmann-La Roche
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:	

U.S. FDA-regulated Device:	
Unapproved/Uncleared Device:	No
IND/IDE Protocol:	No
Human Subjects Review:	Board Status: Approved Approval Number: 07/14/2011 Board Name: Comitato Etico Dell'IRCCS Fondazione S. Raffaele Del Monte Tabor Di Milano Board Affiliation: IRCCS Fondazione S. Raffaele Del Monte Tabor Di Milano Phone: +39 02 26432911 Email: alfredo.anzani@hsr.it Address: via Olgettina, 60 20132 Milano Italy
Data Monitoring:	
Plan to Share IPD:	
FDA Regulated Intervention:	Yes
Section 801 Clinical Trial:	Yes

Study Description

Brief Summary:	This randomized, open-label, crossover study will evaluate participants' preference and healthcare professional (HCP) satisfaction with SC versus IV Herceptin administration in HER2-positive early breast cancer. Participants will be randomized to receive either SC Herceptin or IV Herceptin every 3 weeks for Cycles 1 to 4, followed by crossover to the other treatment administration for Cycles 5 to 8. For up to 10 additional cycles (for a total of 18 cycles), participants will receive IV or SC Herceptin every 3 weeks.
Detailed Description:	

Conditions

Conditions:	Breast Neoplasms
Keywords:	

Study Design

Study Type:	Interventional

Primary Purpose:	Health Services Research
Study Phase:	Phase 2
Interventional Study Model:	Crossover Assignment
Number of Arms:	4
Masking:	No masking
Allocation:	Randomized
Enrollment:	488 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Cohort 1: SC (SID) then IV Herceptin Participants will receive Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin will be administered via single-use injection device (SID), and during Cycles 5 to 8, IV Herceptin will be given. In the continuation period, participants will receive IV Herceptin for up to 10 remaining cycles. Administration will be performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period will be offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP.	Drug: Herceptin Herceptin will be given on Day 1 of each 3-week cycle for a total of 18 cycles. If study treatment for Cycle 1 is IV Herceptin, the initial dose will be a loading dose of 8 milligrams per kilogram (mg/kg) for de novo participants who start Herceptin treatment in the study. For all other cycles where IV Herceptin is given and for non-de novo participants, the dose will be 6 mg/kg. The SC dose will be 600 milligrams (mg) for both the SID and vial formulations for all cycles where SC Herceptin is given. Other Names: • Trastuzumab Device: Single-Use Injection Device The SID will be used, containing Herceptin 600 mg per 5 milliliters (mL).
Experimental: Cohort 1: IV then SC (SID) Herceptin Participants will receive Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin will be given, and during Cycles 5 to 8, SC Herceptin will be administered via SID. In the continuation period, participants will receive IV Herceptin for up to 10 remaining cycles. Administration will be performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period will be offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP.	Drug: Herceptin Herceptin will be given on Day 1 of each 3-week cycle for a total of 18 cycles. If study treatment for Cycle 1 is IV Herceptin, the initial dose will be a loading dose of 8 mg/kg for de novo participants who start Herceptin treatment in the study. For all other cycles where IV Herceptin is given and for non-de novo participants, the dose will be 6 mg/kg. The SC dose will be 600 mg for both the SID and vial formulations for all cycles where SC Herceptin is given. Other Names: • Trastuzumab Device: Single-Use Injection Device The SID will be used, containing Herceptin 600 mg per 5 mL.
Experimental: Cohort 2: SC (Vial) then IV Herceptin Participants will receive Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin will be administered via handheld syringe using the vial formulation, and	Drug: Herceptin Herceptin will be given on Day 1 of each 3-week cycle for a total of 18 cycles. If study treatment for Cycle 1 is IV Herceptin, the initial dose will be a loading dose of 8 mg/kg for de novo participants who start Herceptin

Arms	Assigned Interventions
during Cycles 5 to 8, IV Herceptin will be given. In the continuation period, participants will receive SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration will be performed by HCP throughout the study.	treatment in the study. For all other cycles where IV Herceptin is given and for non-de novo participants, the dose will be 6 mg/kg. The SC dose will be 600 mg for both the SID and vial formulations for all cycles where SC Herceptin is given. Other Names: • Trastuzumab
Experimental: Cohort 2: IV then SC (Vial) Herceptin Participants will receive Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin will be given, and during Cycles 5 to 8, SC Herceptin will be administered via handheld syringe using the vial formulation. In the continuation period, participants will receive SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration will be performed by HCP throughout the study.	Drug: Herceptin Herceptin will be given on Day 1 of each 3-week cycle for a total of 18 cycles. If study treatment for Cycle 1 is IV Herceptin, the initial dose will be a loading dose of 8 mg/kg for de novo participants who start Herceptin treatment in the study. For all other cycles where IV Herceptin is given and for non-de novo participants, the dose will be 6 mg/kg. The SC dose will be 600 mg for both the SID and vial formulations for all cycles where SC Herceptin is given. Other Names: • Trastuzumab

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Sex: Female

Gender Based:

Accepts Healthy Volunteers: No

Criteria: Inclusion Criteria:

- Histologically confirmed HER2-positive primary breast cancer
- No evidence of residual, locally recurrent, or metastatic disease after completion of surgery and chemotherapy (neo-adjuvant or adjuvant)
- Completed neo-adjuvant chemotherapy prior to entry, if received
- At least 8 remaining cycles out of the total 18 planned 3-week cycles, if received IV Herceptin
- Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1

Exclusion Criteria:

- History of other malignancy, except for ductal carcinoma in situ of the breast, curatively treated carcinoma in situ of the cervix, basal cell carcinoma, or other curatively treated malignancies of which the participant has been disease-free for at least 5 years
- Inadequate bone marrow function
- Impaired liver function
- Inadequate renal function
- Serious cardiovascular disease
- Human immunodeficiency virus or hepatitis B or C infection
- Prior maximum cumulative dose of doxorubicin greater than (>) 360 milligrams per meter-squared (mg/m^2) or epirubicin >720 mg/m^2 or equivalent

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Russian Federation
Orenburg, Russian Federation, 460021

St Petersburg, Russian Federation

Irkutsk, Russian Federation, 664035

Moscow, Russian Federation, 115478

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Fuerstenwalde, Germany, 15517

Magedburg, Germany, 39104

Essen, Germany, 45136

Hamburg, Germany, 20246

Recklinghausen, Germany, 45657

Hannover, Germany, 30625

Mainz, Germany, 55131

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Adana, Turkey, 01120

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Eskilstuna, Sweden, 63188

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Sevilla, Sevilla, Spain, 41014

Cordoba, Cordoba, Spain, 14004

Malaga, Malaga, Spain, 29010

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Besancon, France, 25030

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Spain
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References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Pre-Assignment Details	A total of 248 participants were randomized into the study in Cohort 1 (of whom 244 were treated) and 240 participants were randomized into the study in Cohort 2 (of whom 239 were treated). Those participants who did not receive any treatment were not included in the treatment periods of the Participant Flow.

Reporting Groups

	Description
Cohort 1: SC (SID) Then IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin was administered via single-use injection device (SID), and during Cycles 5 to 8, IV Herceptin was given. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by healthcare professional (HCP). Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The SC dose was 600 milligrams (mg) for all cycles where SC Herceptin was given, and the IV dose was 6 milligrams per kilogram (mg/kg) for all cycles where IV Herceptin was given.

	Description
Cohort 1: IV Then SC (SID) Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin was given, and during Cycles 5 to 8, SC Herceptin was administered via SID. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The IV dose was a loading dose of 8 mg/kg in Cycle 1 for de novo participants who started Herceptin treatment in the study, and a dose of 6 mg/kg for all subsequent cycles where IV Herceptin was given and for non-de novo participants. The SC dose was 600 mg for all cycles where SC Herceptin was given.
Cohort 2: SC (Vial) Then IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin was administered via handheld syringe using the vial formulation, and during Cycles 5 to 8, IV Herceptin was given. In the continuation period, participants received SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration was performed by HCP throughout the study. The SC dose was 600 mg for all cycles where SC Herceptin was given, and the IV dose was 6 mg/kg for all cycles where IV Herceptin was given.
Cohort 2: IV Then SC (Vial) Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin was given, and during Cycles 5 to 8, SC Herceptin was administered via handheld syringe using the vial formulation. In the continuation period, participants received SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration was performed by HCP throughout the study. The IV dose was a loading dose of 8 mg/kg in Cycle 1 for de novo participants who started Herceptin treatment in the study, and a dose of 6 mg/kg for all subsequent cycles where IV Herceptin was given and for non-de novo participants. The SC dose was 600 mg for all cycles where SC Herceptin was given.

Crossover Treatment 1 (Cycles 1 to 4)

	Cohort 1: SC (SID) Then IV Herceptin	Cohort 1: IV Then SC (SID) Herceptin	Cohort 2: SC (Vial) Then IV Herceptin	Cohort 2: IV Then SC (Vial) Herceptin
Started	122 [1]	122 [1]	121 [2]	118 [3]
Completed	119	120	119	116
Not Completed	3	2	2	2

[1] A total of 124 participants were randomized, but 2 did not receive any treatment.
[2] A total of 121 participants were randomized who all received study treatment.
[3] A total of 119 participants were randomized, but 1 did not receive any treatment.

Crossover Treatment 2 (Cycles 5 to 8)

	Cohort 1: SC (SID) Then IV Herceptin	Cohort 1: IV Then SC (SID) Herceptin	Cohort 2: SC (Vial) Then IV Herceptin	Cohort 2: IV Then SC (Vial) Herceptin
Started	119	120	119	116

	Cohort 1: SC (SID) Then IV Herceptin	Cohort 1: IV Then SC (SID) Herceptin	Cohort 2: SC (Vial) Then IV Herceptin	Cohort 2: IV Then SC (Vial) Herceptin
Completed	113	116	107	105
Not Completed	6	4	12	11

Continuation Treatment (Cycles 9 to 18)

	Cohort 1: SC (SID) Then IV Herceptin	Cohort 1: IV Then SC (SID) Herceptin	Cohort 2: SC (Vial) Then IV Herceptin	Cohort 2: IV Then SC (Vial) Herceptin
Started	113	116	107	105
Completed	109	109	105	102
Not Completed	4	7	2	3

Safety Follow-Up Period

	Cohort 1: SC (SID) Then IV Herceptin	Cohort 1: IV Then SC (SID) Herceptin	Cohort 2: SC (Vial) Then IV Herceptin	Cohort 2: IV Then SC (Vial) Herceptin
Started	124 [1]	124 [1]	121 [2]	119 [3]
Completed	99	106	104	100
Not Completed	25	18	17	19

[1] All 124 randomized participants entered follow-up regardless of whether they received treatment.
[2] All 121 randomized participants entered follow-up regardless of whether they received treatment.
[3] All 119 randomized participants entered follow-up regardless of whether they received treatment.

Baseline Characteristics

Baseline Analysis Population Description
Safety Population: All participants who received at least one dose of Herceptin.

Reporting Groups

	Description
Cohort 1 Overall: SC (SID) and IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles, randomized to one of two crossover sequences: SC Herceptin via SID for Cycles 1 to 4 followed by IV Herceptin for Cycles 5 to 8, or vice versa. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. If study treatment for Cycle 1 was IV Herceptin, the initial dose was a loading dose of 8 mg/kg for de novo participants who started Herceptin treatment in the study. For all other cycles where IV Herceptin was given and for non-de novo participants, the dose was 6 mg/kg. The SC dose was 600 mg for all cycles where SC Herceptin was given.
Cohort 2 Overall: SC (Vial) and IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles, randomized to one of two crossover sequences: SC Herceptin via handheld syringe using the vial formulation for Cycles 1 to 4 followed by IV Herceptin for Cycles 5 to 8, or vice versa. In the continuation period, participants received SC Herceptin for up to 10 remaining cycles. Administration was performed by HCP throughout the study. If study treatment for Cycle 1 was IV Herceptin, the initial dose was a loading dose of 8 mg/kg for de novo participants who started Herceptin treatment in the study. For all other cycles where IV Herceptin was given and for non-de novo participants, the dose was 6 mg/kg. The SC dose was 600 mg for all cycles where SC Herceptin was given.

Baseline Measures

		Cohort 1 Overall: SC (SID) and IV Herceptin	Cohort 2 Overall: SC (Vial) and IV Herceptin	Total
Overall Number of Participants		244	239	483
Age, Continuous Mean (Standard Deviation) Unit of measure: years	Number Analyzed	244 participants	239 participants	483 participants
		53.3 (11.40)	52.9 (10.87)	53.1 (11.13)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	244 participants	239 participants	483 participants
	Female	244 100%	239 100%	483 100%
	Male	0 0%	0 0%	0 0%

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants by Preferred Method of Drug Administration

Measure Description	The preferred method of drug administration (IV or SC Herceptin) was assessed in trial-specific telephone interviews with each study participant. Participants were asked, “All things considered, which method of administration did you prefer?” at the end of the crossover period (Week 24). The percentage of participants who preferred each method of drug administration was reported.
Time Frame	Week 24

Analysis Population Description

Intent-to-Treat (ITT) Population: All participants who received both IV and SC Herceptin and who completed the trial-specific telephone interview conducted after the end of the crossover period.

Reporting Groups

	Description
Cohort 1: SC (SID) Then IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin was administered via SID, and during Cycles 5 to 8, IV Herceptin was given. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The SC dose was 600 mg for all cycles where SC Herceptin was given, and the IV dose was 6 mg/kg for all cycles where IV Herceptin was given.
Cohort 1: IV Then SC (SID) Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin was given, and during Cycles 5 to 8, SC Herceptin was administered via SID. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The IV dose was a loading dose of 8 mg/kg in Cycle 1 for de novo participants who started Herceptin treatment in the study, and a dose of 6 mg/kg for all subsequent cycles where IV Herceptin was given and for non-de novo participants. The SC dose was 600 mg for all cycles where SC Herceptin was given.
Cohort 2: SC (Vial) Then IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin was administered via handheld syringe using the vial formulation, and during Cycles 5 to 8, IV Herceptin was given. In the continuation period, participants received SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration was performed by HCP throughout the study. The SC dose was 600 mg for all cycles where SC Herceptin was given, and the IV dose was 6 mg/kg for all cycles where IV Herceptin was given.
Cohort 2: IV Then SC (Vial) Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin was given, and during Cycles 5 to 8, SC Herceptin was administered via handheld syringe using the vial formulation. In the continuation period, participants received SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration was performed by HCP throughout the study. The IV dose was a loading dose of 8 mg/kg in Cycle 1 for de novo participants who started Herceptin treatment in the study, and a dose of 6 mg/kg for all subsequent cycles where IV Herceptin was given and for non-de novo participants. The SC dose was 600 mg for all cycles where SC Herceptin was given.

Measured Values

	Cohort 1: SC (SID) Then IV Herceptin	Cohort 1: IV Then SC (SID) Herceptin	Cohort 2: SC (Vial) Then IV Herceptin	Cohort 2: IV Then SC (Vial) Herceptin
Overall Number of Participants Analyzed	117	119	118	113
Percentage of Participants by Preferred Method of Drug Administration Measure Type: Number Unit of measure: percentage of participants				
SC Herceptin	95.7	87.4	83.9	88.5
IV Herceptin	4.3	9.2	13.6	11.5
No Preference	0.0	3.4	2.5	0.0

Statistical Analysis 1 for Percentage of Participants by Preferred Method of Drug Administration

Statistical Analysis Overview	Comparison Group Selection	Cohort 1: SC (SID) Then IV Herceptin
	Comments	[Not specified]
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other [Estimated Proportion]
	Estimated Value	0.957
	Confidence Interval	(2-Sided) 95% 0.903 to 0.986
	Estimation Comments	The estimated proportion of participants who preferred SC Herceptin and the corresponding exact binomial confidence interval (CI) were determined.

Statistical Analysis 2 for Percentage of Participants by Preferred Method of Drug Administration

Statistical Analysis Overview	Comparison Group Selection	Cohort 1: SC (SID) Then IV Herceptin
	Comments	[Not specified]
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Other [Estimated Proportion]

	Estimated Value	0.964
	Confidence Interval	(2-Sided) 95% 0.908 to 0.986
	Estimation Comments	The estimated proportion of participants who preferred SC Herceptin and the corresponding CI were determined using logistic regression with factors of previous Herceptin status and treatment.

Statistical Analysis 3 for Percentage of Participants by Preferred Method of Drug Administration

Statistical Analysis Overview	Comparison Group Selection	Cohort 1: IV Then SC (SID) Herceptin
	Comments	[Not specified]
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Estimated Proportion]
	Estimated Value	0.874
	Confidence Interval	(2-Sided) 95% 0.801 to 0.928
	Estimation Comments	The estimated proportion of participants who preferred SC Herceptin and the corresponding exact binomial CI were determined.

Statistical Analysis 4 for Percentage of Participants by Preferred Method of Drug Administration

Statistical Analysis Overview	Comparison Group Selection	Cohort 1: IV Then SC (SID) Herceptin
	Comments	[Not specified]
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Estimated Proportion]
	Estimated Value	0.892
	Confidence Interval	(2-Sided) 95% 0.804 to 0.943
	Estimation Comments	The estimated proportion of participants who preferred SC Herceptin and the corresponding CI were determined using logistic regression with factors of previous Herceptin status and treatment.

Statistical Analysis 5 for Percentage of Participants by Preferred Method of Drug Administration

Statistical Analysis Overview	Comparison Group Selection	Cohort 2: SC (Vial) Then IV Herceptin
	Comments	[Not specified]
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Estimated Proportion]
	Estimated Value	0.839
	Confidence Interval	(2-Sided) 95% 0.760 to 0.900
	Estimation Comments	The estimated proportion of participants who preferred SC Herceptin and the corresponding exact binomial CI were determined.

Statistical Analysis 6 for Percentage of Participants by Preferred Method of Drug Administration

Statistical Analysis Overview	Comparison Group Selection	Cohort 2: SC (Vial) Then IV Herceptin
	Comments	[Not specified]
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Estimated Proportion]
	Estimated Value	0.874
	Confidence Interval	(2-Sided) 95% 0.776 to 0.933
	Estimation Comments	The estimated proportion of participants who preferred SC Herceptin and the corresponding CI were determined using logistic regression with factors of previous Herceptin status and treatment.

Statistical Analysis 7 for Percentage of Participants by Preferred Method of Drug Administration

Statistical Analysis Overview	Comparison Group Selection	Cohort 2: IV Then SC (Vial) Herceptin
	Comments	[Not specified]
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Estimated Proportion]
	Estimated Value	0.885

	Confidence Interval	(2-Sided) 95% 0.811 to 0.937
	Estimation Comments	The estimated proportion of participants who preferred SC Herceptin and the corresponding exact binomial CI were determined.

Statistical Analysis 8 for Percentage of Participants by Preferred Method of Drug Administration

Statistical Analysis Overview	Comparison Group Selection	Cohort 2: IV Then SC (Vial) Herceptin
	Comments	[Not specified]
	Type of Statistical Test	Superiority or Other (legacy)
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Estimated Proportion]
	Estimated Value	0.911
	Confidence Interval	(2-Sided) 95% 0.827 to 0.956
	Estimation Comments	The estimated proportion of participants who preferred SC Herceptin and the corresponding CI were determined using logistic regression with factors of previous Herceptin status and treatment.

2. Secondary Outcome Measure:

Measure Title	Percentage of HCPs by Most Satisfied Method of Drug Administration
Measure Description	The method of drug administration with which HCPs were most satisfied (IV or SC Herceptin) was assessed via questionnaire with each HCP using the question, “All things considered, with which method of administration were you most satisfied?” at the end of the crossover period (Week 24). The percentage of HCPs who were most satisfied with each method of drug administration was reported.
Time Frame	Week 24

Analysis Population Description

HCP Population: All HCPs who participated in the study and completed the HCP questionnaire. Results were planned to be analyzed for all HCPs combined because the objective of the study was to compare preference between SC and IV Herceptin.

Reporting Groups

	Description
All HCPs: SC and IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles, randomized to one of two crossover sequences: SC Herceptin via SID (Cohort 1) or vial (Cohort 2) for Cycles 1 to 4 followed by IV Herceptin for Cycles 5 to 8, or vice versa. In the continuation period, participants received IV Herceptin (Cohort 1) or SC Herceptin (Cohort 2) for up to 10 remaining cycles. Participants in Cohort 1 with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered to self-administer SC Herceptin via SID under the direction of a trained HCP, whereas in Cohort 2, administration was performed by HCP throughout the study. If study treatment for Cycle 1 was IV Herceptin, the initial dose was a loading dose of 8 mg/kg for de novo participants who started Herceptin treatment in the study. For all other cycles where IV Herceptin was given and for non-de novo participants, the dose was 6 mg/kg. The SC dose was 600 mg for both SID and vial.

Measured Values

	All HCPs: SC and IV Herceptin
Overall Number of Participants Analyzed	235
Overall Number of Units Analyzed Type of Units Analyzed: HCPs	235
Percentage of HCPs by Most Satisfied Method of Drug Administration Measure Type: Number Unit of measure: percentage of HCPs	
SC Herceptin	77.0
IV Herceptin	3.0
No Preference	20.0

3. Secondary Outcome Measure:

Measure Title	Percentage of HCPs by Time Required to Perform Each Method of Drug Administration
Measure Description	The time required to perform each method of drug administration was assessed via questionnaire with each HCP by asking to rate the amount of time it took to administer each method of drug administration (IV or SC Herceptin) at the end of the crossover period (Week 24). Time was rated in the following time block categories: less than (<) 5 minutes, 6 to 10 minutes, 11 to 15 minutes, 16 to 20 minutes, and greater than (>) 20 minutes. Responses of "Not Sure" and "Unknown" were also allowed. The percentage of HCPs who rated the amount of time in each of the categories was reported.
Time Frame	Week 24

Analysis Population Description

HCP Population. Results were planned to be analyzed for all HCPs combined because the objective of the study was to compare HCP perceived time savings with use of SC over IV Herceptin.

Reporting Groups

	Description
All HCPs: SC and IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles, randomized to one of two crossover sequences: SC Herceptin via SID (Cohort 1) or vial (Cohort 2) for Cycles 1 to 4 followed by IV Herceptin for Cycles 5 to 8, or vice versa. In the continuation period, participants received IV Herceptin (Cohort 1) or SC Herceptin (Cohort 2) for up to 10 remaining cycles. Participants in Cohort 1 with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered to self-administer SC Herceptin via SID under the direction of a trained HCP, whereas in Cohort 2, administration was performed by HCP throughout the study. If study treatment for Cycle 1 was IV Herceptin, the initial dose was a loading dose of 8 mg/kg for de novo participants who started Herceptin treatment in the study. For all other cycles where IV Herceptin was given and for non-de novo participants, the dose was 6 mg/kg. The SC dose was 600 mg for both SID and vial.

Measured Values

	All HCPs: SC and IV Herceptin
Overall Number of Participants Analyzed	235
Overall Number of Units Analyzed Type of Units Analyzed: HCPs	235
Percentage of HCPs by Time Required to Perform Each Method of Drug Administration Measure Type: Number Unit of measure: percentage of HCPs	
SC Herceptin, <5 minutes	44.3
SC Herceptin, 6 to 10 minutes	46.4
SC Herceptin, 11 to 15 minutes	3.4
SC Herceptin, 16 to 20 minutes	0.4
SC Herceptin, >20 minutes	0.4
SC Herceptin, Not Sure	0.0
SC Herceptin, Unknown	5.1
IV Herceptin, <5 minutes	11.1
IV Herceptin, 6 to 10 minutes	9.8
IV Herceptin, 11 to 15 minutes	3.8

	All HCPs: SC and IV Herceptin
IV Herceptin, 16 to 20 minutes	44.3
IV Herceptin, >20 minutes	22.1
IV Herceptin, Not Sure	5.1
IV Herceptin, Unknown	3.8

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With an Event-Free Survival (EFS) Event
Measure Description	EFS events included local, regional, or distant recurrence of the original breast cancer, occurrence of contralateral breast cancer, or death due to any cause. The percentage of participants who had an EFS event at any time on study was reported.
Time Frame	From Baseline until time of event; assessed every 6 months (median follow-up of 3 years)

Analysis Population Description

ITT Population

Reporting Groups

	Description
Cohort 1: SC (SID) Then IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin was administered via SID, and during Cycles 5 to 8, IV Herceptin was given. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The SC dose was 600 mg for all cycles where SC Herceptin was given, and the IV dose was 6 mg/kg for all cycles where IV Herceptin was given.
Cohort 1: IV Then SC (SID) Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin was given, and during Cycles 5 to 8, SC Herceptin was administered via SID. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The IV dose was a loading dose of 8 mg/kg in Cycle 1 for de novo participants who started Herceptin treatment in the study, and a dose of 6 mg/kg for all subsequent cycles where IV Herceptin was given and for non-de novo participants. The SC dose was 600 mg for all cycles where SC Herceptin was given.

	Description
Cohort 2: SC (Vial) Then IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin was administered via handheld syringe using the vial formulation, and during Cycles 5 to 8, IV Herceptin was given. In the continuation period, participants received SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration was performed by HCP throughout the study. The SC dose was 600 mg for all cycles where SC Herceptin was given, and the IV dose was 6 mg/kg for all cycles where IV Herceptin was given.
Cohort 2: IV Then SC (Vial) Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin was given, and during Cycles 5 to 8, SC Herceptin was administered via handheld syringe using the vial formulation. In the continuation period, participants received SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration was performed by HCP throughout the study. The IV dose was a loading dose of 8 mg/kg in Cycle 1 for de novo participants who started Herceptin treatment in the study, and a dose of 6 mg/kg for all subsequent cycles where IV Herceptin was given and for non-de novo participants. The SC dose was 600 mg for all cycles where SC Herceptin was given.

Measured Values

	Cohort 1: SC (SID) Then IV Herceptin	Cohort 1: IV Then SC (SID) Herceptin	Cohort 2: SC (Vial) Then IV Herceptin	Cohort 2: IV Then SC (Vial) Herceptin
Overall Number of Participants Analyzed	117	119	118	113
Percentage of Participants With an Event-Free Survival (EFS) Event Measure Type: Number Unit of measure: percentage of participants	13.7	6.7	11.9	7.1

5. Secondary Outcome Measure:

Measure Title	Duration of EFS According to Kaplan-Meier Estimate
Measure Description	EFS was defined as the time from randomization to a local, regional, or distant recurrence of the original breast cancer, occurrence of contralateral breast cancer, or death due to any cause. The median duration of EFS and corresponding 95 percent (%) CI according to Kaplan-Meier estimates were planned to be reported and expressed in months.
Time Frame	From Baseline until time of event; assessed every 6 months (median follow-up of 3 years)

Analysis Population Description

ITT Population

Reporting Groups

	Description
Cohort 1: SC (SID) Then IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin was administered via SID, and during Cycles 5 to 8, IV Herceptin was given. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The SC dose was 600 mg for all cycles where SC Herceptin was given, and the IV dose was 6 mg/kg for all cycles where IV Herceptin was given.
Cohort 1: IV Then SC (SID) Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin was given, and during Cycles 5 to 8, SC Herceptin was administered via SID. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The IV dose was a loading dose of 8 mg/kg in Cycle 1 for de novo participants who started Herceptin treatment in the study, and a dose of 6 mg/kg for all subsequent cycles where IV Herceptin was given and for non-de novo participants. The SC dose was 600 mg for all cycles where SC Herceptin was given.
Cohort 2: SC (Vial) Then IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin was administered via handheld syringe using the vial formulation, and during Cycles 5 to 8, IV Herceptin was given. In the continuation period, participants received SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration was performed by HCP throughout the study. The SC dose was 600 mg for all cycles where SC Herceptin was given, and the IV dose was 6 mg/kg for all cycles where IV Herceptin was given.
Cohort 2: IV Then SC (Vial) Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin was given, and during Cycles 5 to 8, SC Herceptin was administered via handheld syringe using the vial formulation. In the continuation period, participants received SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration was performed by HCP throughout the study. The IV dose was a loading dose of 8 mg/kg in Cycle 1 for de novo participants who started Herceptin treatment in the study, and a dose of 6 mg/kg for all subsequent cycles where IV Herceptin was given and for non-de novo participants. The SC dose was 600 mg for all cycles where SC Herceptin was given.

Measured Values

	Cohort 1: SC (SID) Then IV Herceptin	Cohort 1: IV Then SC (SID) Herceptin	Cohort 2: SC (Vial) Then IV Herceptin	Cohort 2: IV Then SC (Vial) Herceptin
Overall Number of Participants Analyzed	117	119	118	113
Duration of EFS According to Kaplan-Meier Estimate Median (95% Confidence Interval) Unit of measure: months	NA (NA to NA) [1]	NA (42.0 to NA) [1]	NA (NA to NA) [1]	NA (NA to NA) [1]

[1] Median and 95% CI not presented due to insufficient follow-up to allow estimation.

6. Secondary Outcome Measure:

Measure Title	3-Year EFS Rate
Measure Description	EFS events included local, regional, or distant recurrence of the original breast cancer, occurrence of contralateral breast cancer, or death due to any cause. The proportion of participants without an EFS event (i.e., the EFS rate) and corresponding 95% CI at 3 years after randomization was reported.
Time Frame	Year 3

Analysis Population Description

ITT Population

Reporting Groups

	Description
Cohort 1: SC (SID) Then IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin was administered via SID, and during Cycles 5 to 8, IV Herceptin was given. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The SC dose was 600 mg for all cycles where SC Herceptin was given, and the IV dose was 6 mg/kg for all cycles where IV Herceptin was given.
Cohort 1: IV Then SC (SID) Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin was given, and during Cycles 5 to 8, SC Herceptin was administered via SID. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The IV dose was a loading dose of 8 mg/kg in Cycle 1 for de novo participants who started Herceptin treatment in the study, and a dose of 6 mg/kg for all subsequent cycles where IV Herceptin was given and for non-de novo participants. The SC dose was 600 mg for all cycles where SC Herceptin was given.
Cohort 2: SC (Vial) Then IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin was administered via handheld syringe using the vial formulation, and during Cycles 5 to 8, IV Herceptin was given. In the continuation period, participants received SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration was performed by HCP throughout the study. The SC dose was 600 mg for all cycles where SC Herceptin was given, and the IV dose was 6 mg/kg for all cycles where IV Herceptin was given.

	Description
Cohort 2: IV Then SC (Vial) Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin was given, and during Cycles 5 to 8, SC Herceptin was administered via handheld syringe using the vial formulation. In the continuation period, participants received SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration was performed by HCP throughout the study. The IV dose was a loading dose of 8 mg/kg in Cycle 1 for de novo participants who started Herceptin treatment in the study, and a dose of 6 mg/kg for all subsequent cycles where IV Herceptin was given and for non-de novo participants. The SC dose was 600 mg for all cycles where SC Herceptin was given.

Measured Values

	Cohort 1: SC (SID) Then IV Herceptin	Cohort 1: IV Then SC (SID) Herceptin	Cohort 2: SC (Vial) Then IV Herceptin	Cohort 2: IV Then SC (Vial) Herceptin
Overall Number of Participants Analyzed	117	119	118	113
3-Year EFS Rate Number (95% Confidence Interval) Unit of measure: proportion of participants	0.849 (0.763 to 0.906)	0.948 (0.887 to 0.976)	0.886 (0.811 to 0.932)	0.937 (0.873 to 0.970)

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Responses of "Agree" or "Strongly Agree" on the SC SID Satisfaction Questionnaire
Measure Description	Participants who performed self-administration of SC Herceptin via SID were given an evaluation questionnaire during the continuation period (Weeks 25 to 52) after their first self-administration. Participants responded to 5 statements about their comfort with self-injection, the convenience of the SID, their self-confidence using the SID, their satisfaction with the SID, and whether they would consider using the SID again in the future. Each statement used a 5-item rating scale with responses from “Strongly Disagree” to “Strongly Agree”. The percentage of participants with a positive response (either “Agree” or “Strongly Agree”) to each questionnaire statement was reported.
Time Frame	Immediately following first self-administration of SC Herceptin via SID (once during Weeks 25 to 52)

Analysis Population Description

Safety Population. The "Number of Participants Analyzed" reflects those who self-administered SC Herceptin using the SID and completed the SC SID questionnaire. Results were planned to be analyzed for only Cohort 1 because the objective of the study was to evaluate satisfaction among those who self-administered the SID formulation of Herceptin.

Reporting Groups

	Description
Cohort 1: SC (SID) Then IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin was administered via SID, and during Cycles 5 to 8, IV Herceptin was given. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The SC dose was 600 mg for all cycles where SC Herceptin was given, and the IV dose was 6 mg/kg for all cycles where IV Herceptin was given.
Cohort 1: IV Then SC (SID) Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin was given, and during Cycles 5 to 8, SC Herceptin was administered via SID. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The IV dose was a loading dose of 8 mg/kg in Cycle 1 for de novo participants who started Herceptin treatment in the study, and a dose of 6 mg/kg for all subsequent cycles where IV Herceptin was given and for non-de novo participants. The SC dose was 600 mg for all cycles where SC Herceptin was given.

Measured Values

	Cohort 1: SC (SID) Then IV Herceptin	Cohort 1: IV Then SC (SID) Herceptin
Overall Number of Participants Analyzed	19	15
Percentage of Participants With Responses of "Agree" or "Strongly Agree" on the SC SID Satisfaction Questionnaire Measure Type: Number Unit of measure: percentage of participants		
Comfortable	94.7	86.7
Convenient	100	100
Confident	100	100
Satisfied	100	93.3
Would Use Again	100	93.3

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Anti-Trastuzumab or Anti-Recombinant Human Hyaluronidase (rHuPH20) Antibodies

Measure Description	Participants in Cohort 1 provided blood samples for immunogenicity testing to assess for anti-drug antibodies (ADAs) to trastuzumab or rHuPH20, a component of the SC Herceptin formulation. The percentage of participants who were trastuzumab ADA-positive and the percentage of participants who were rHuPH20 ADA-positive were each reported.
Time Frame	Baseline, pre-dose (0 hours) during Cycle 5 (cycle length of 3 weeks)

Analysis Population Description

Safety Population. Results were planned to be analyzed for only Cohort 1 because the objective of the study was to evaluate immunogenicity within participants who received the SID formulation of Herceptin. The number of participants who provided ADA samples at each timepoint (n) is shown in the table.

Reporting Groups

	Description
Cohort 1: SC (SID) Then IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, SC Herceptin was administered via SID, and during Cycles 5 to 8, IV Herceptin was given. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The SC dose was 600 mg for all cycles where SC Herceptin was given, and the IV dose was 6 mg/kg for all cycles where IV Herceptin was given.
Cohort 1: IV Then SC (SID) Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. During Cycles 1 to 4 of the crossover period, IV Herceptin was given, and during Cycles 5 to 8, SC Herceptin was administered via SID. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. The IV dose was a loading dose of 8 mg/kg in Cycle 1 for de novo participants who started Herceptin treatment in the study, and a dose of 6 mg/kg for all subsequent cycles where IV Herceptin was given and for non-de novo participants. The SC dose was 600 mg for all cycles where SC Herceptin was given.

Measured Values

	Cohort 1: SC (SID) Then IV Herceptin	Cohort 1: IV Then SC (SID) Herceptin
Overall Number of Participants Analyzed	122	122
Percentage of Participants With Anti-Trastuzumab or Anti-Recombinant Human Hyaluronidase (rHuPH20) Antibodies Measure Type: Number Unit of measure: percentage of participants		
Trastuzumab ADA-Positive, Baseline (n=120,121)	2.5	4.1
Trastuzumab ADA-Positive, Cycle 5 (n=114,119)	0	3.4

	Cohort 1: SC (SID) Then IV Herceptin	Cohort 1: IV Then SC (SID) Herceptin
rHuPH20 ADA-Positive, Baseline (n=120,121)	5.8	7.4
rHuPH20 ADA-Positive, Cycle 5 (n=115,119)	2.6	7.6

Reported Adverse Events

Time Frame	During treatment from Cycles 1 to 8 (crossover period) and Cycles 9 to 18 (continuation period); cycle length of 3 weeks
Adverse Event Reporting Description	Analysis Population Description: Safety Population

Reporting Groups

	Description
Cohort 1: SC (SID) Herceptin (Crossover)	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. SC Herceptin was administered via SID as a 600-mg dose during four consecutive cycles of the crossover period. Administration was performed by HCP.
Cohort 1: IV Herceptin (Crossover)	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. IV Herceptin was given as a 6-mg/kg dose during four consecutive cycles of the crossover period. If study treatment for Cycle 1 was IV Herceptin, the initial dose was a loading dose of 8 mg/kg (instead of 6 mg/kg) for de novo participants who started Herceptin treatment in the study. Administration was performed by HCP.
Cohort 1: IV Herceptin (Continuation)	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. In the continuation period, participants received IV Herceptin as a 6-mg/kg dose for up to 10 remaining cycles. Administration was performed by HCP.
Cohort 1: SC (SID) Herceptin (Continuation)	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID as a 600-mg dose under the direction of a trained HCP.
Cohort 1 Overall: SC (SID) and IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles, randomized to one of two crossover sequences: SC Herceptin via SID for Cycles 1 to 4 followed by IV Herceptin for Cycles 5 to 8, or vice versa. In the continuation period, participants received IV Herceptin for up to 10 remaining cycles. Administration was performed by HCP. Those with at least 2 treatment cycles remaining of the 18-cycle treatment course after the crossover period were offered the opportunity to self-administer SC Herceptin via SID under the direction of a trained HCP. If study treatment for Cycle 1 was IV Herceptin, the initial dose was a loading dose of 8 mg/kg for de novo participants who started Herceptin treatment in the study. For all other cycles where IV Herceptin was given and for non-de novo participants, the dose was 6 mg/kg. The SC dose was 600 mg for all cycles where SC Herceptin was given.

	Description
Cohort 2: SC (Vial) Herceptin (Crossover)	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. SC Herceptin was administered via handheld syringe using the vial formulation as a 600-mg dose during four consecutive cycles of the crossover period. Administration was performed by HCP.
Cohort 2: IV Herceptin (Crossover)	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. IV Herceptin was given as a 6-mg/kg dose during four consecutive cycles of the crossover period. If study treatment for Cycle 1 was IV Herceptin, the initial dose was a loading dose of 8 mg/kg (instead of 6 mg/kg) for de novo participants who started Herceptin treatment in the study. Administration was performed by HCP.
Cohort 2: IV Herceptin (Continuation)	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. In the continuation period, participants were planned to receive SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. However, under protocol deviation a small number of participants received IV Herceptin as a 6-mg/kg dose for this period. Administration was performed by HCP.
Cohort 2: SC (Vial) Herceptin (Continuation)	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles. In the continuation period, participants received SC Herceptin via handheld syringe using the vial formulation for up to 10 remaining cycles. Administration was performed by HCP.
Cohort 2 Overall: SC (Vial) and IV Herceptin	Participants received Herceptin on Day 1 of each 3-week cycle for 18 cycles, randomized to one of two crossover sequences: SC Herceptin via handheld syringe using the vial formulation for Cycles 1 to 4 followed by IV Herceptin for Cycles 5 to 8, or vice versa. In the continuation period, participants received SC Herceptin for up to 10 remaining cycles. Administration was performed by HCP throughout the study. If study treatment for Cycle 1 was IV Herceptin, the initial dose was a loading dose of 8 mg/kg for de novo participants who started Herceptin treatment in the study. For all other cycles where IV Herceptin was given and for non-de novo participants, the dose was 6 mg/kg. The SC dose was 600 mg for all cycles where SC Herceptin was given.

All-Cause Mortality

	Cohort 1: SC (SID) Herceptin (Crossover)	Cohort 1: IV Herceptin (Crossover)	Cohort 1: IV Herceptin (Continuation)	Cohort 1: SC (SID) Herceptin (Continuation)	Cohort 1 Overall: SC (SID) and IV Herceptin	Cohort 2: SC (Vial) Herceptin (Crossover)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total All-Cause Mortality	/	/	/	/	/	/

	Cohort 2: IV Herceptin (Crossover)	Cohort 2: IV Herceptin (Continuation)	Cohort 2: SC (Vial) Herceptin (Continuation)	Cohort 2 Overall: SC (Vial) and IV Herceptin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total All-Cause Mortality	/	/	/	/

Serious Adverse Events

	Cohort 1: SC (SID) Herceptin (Crossover)	Cohort 1: IV Herceptin (Crossover)	Cohort 1: IV Herceptin (Continuation)	Cohort 1: SC (SID) Herceptin (Continuation)	Cohort 1 Overall: SC (SID) and IV Herceptin	Cohort 2: SC (Vial) Herceptin (Crossover)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	4/242 (1.65%)	2/241 (0.83%)	6/226 (2.65%)	1/43 (2.33%)	12/244 (4.92%)	0/237 (0%)
Cardiac disorders						
Left ventricular dysfunction [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	0/237 (0%)
General disorders						
Adverse drug reaction [A] *	0/242 (0%)	0/241 (0%)	1/226 (0.44%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)
Chest pain [A] *	0/242 (0%)	0/241 (0%)	1/226 (0.44%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)
Hepatobiliary disorders						
Cholelithiasis [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	0/237 (0%)
Infections and infestations						
Breast abscess [A] *	0/242 (0%)	0/241 (0%)	1/226 (0.44%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)
Device related infection [A] *	1/242 (0.41%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)
Influenza [A] *	0/242 (0%)	1/241 (0.41%)	0/226 (0%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)
Postoperative wound infection [A] *	0/242 (0%)	0/241 (0%)	1/226 (0.44%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)
Pyelonephritis [A] *	0/242 (0%)	0/241 (0%)	1/226 (0.44%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)
Subcutaneous abscess [A] *	1/242 (0.41%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)
Wound infection [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	0/237 (0%)
Injury, poisoning and procedural complications						
Suture related complication [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	0/237 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Adenoma benign [A] *	1/242 (0.41%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)
Cerebral haemangioma [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	1/43 (2.33%)	1/244 (0.41%)	0/237 (0%)

	Cohort 1: SC (SID) Herceptin (Crossover)	Cohort 1: IV Herceptin (Crossover)	Cohort 1: IV Herceptin (Continuation)	Cohort 1: SC (SID) Herceptin (Continuation)	Cohort 1 Overall: SC (SID) and IV Herceptin	Cohort 2: SC (Vial) Herceptin (Crossover)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Nervous system disorders						
Dizziness [A] *	0/242 (0%)	0/241 (0%)	1/226 (0.44%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)
Psychiatric disorders						
Mental disorder [A] *	0/242 (0%)	1/241 (0.41%)	0/226 (0%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)
Reproductive system and breast disorders						
Endometrial hypertrophy [A] *	0/242 (0%)	0/241 (0%)	1/226 (0.44%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)
Surgical and medical procedures						
Breast reconstruction [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	0/237 (0%)
Knee arthroplasty [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	0/237 (0%)
Mammoplasty [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	0/237 (0%)
Vascular disorders						
Haematoma [A] *	1/242 (0.41%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	1/244 (0.41%)	0/237 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (18.1)

	Cohort 2: IV Herceptin (Crossover)	Cohort 2: IV Herceptin (Continuation)	Cohort 2: SC (Vial) Herceptin (Continuation)	Cohort 2 Overall: SC (Vial) and IV Herceptin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	2/237 (0.84%)	0/10 (0%)	5/208 (2.4%)	7/239 (2.93%)
Cardiac disorders				
Left ventricular dysfunction [A] *	0/237 (0%)	0/10 (0%)	1/208 (0.48%)	1/239 (0.42%)
General disorders				
Adverse drug reaction [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)

	Cohort 2: IV Herceptin (Crossover)	Cohort 2: IV Herceptin (Continuation)	Cohort 2: SC (Vial) Herceptin (Continuation)	Cohort 2 Overall: SC (Vial) and IV Herceptin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Chest pain [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Hepatobiliary disorders				
Cholelithiasis [A] *	1/237 (0.42%)	0/10 (0%)	0/208 (0%)	1/239 (0.42%)
Infections and infestations				
Breast abscess [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Device related infection [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Influenza [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Postoperative wound infection [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Pyelonephritis [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Subcutaneous abscess [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Wound infection [A] *	1/237 (0.42%)	0/10 (0%)	1/208 (0.48%)	2/239 (0.84%)
Injury, poisoning and procedural complications				
Suture related complication [A] *	1/237 (0.42%)	0/10 (0%)	0/208 (0%)	1/239 (0.42%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Adenoma benign [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Cerebral haemangioma [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Nervous system disorders				
Dizziness [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Psychiatric disorders				
Mental disorder [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Reproductive system and breast disorders				
Endometrial hypertrophy [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Surgical and medical procedures				

	Cohort 2: IV Herceptin (Crossover)	Cohort 2: IV Herceptin (Continuation)	Cohort 2: SC (Vial) Herceptin (Continuation)	Cohort 2 Overall: SC (Vial) and IV Herceptin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Breast reconstruction [A] *	0/237 (0%)	0/10 (0%)	1/208 (0.48%)	1/239 (0.42%)
Knee arthroplasty [A] *	0/237 (0%)	0/10 (0%)	1/208 (0.48%)	1/239 (0.42%)
Mammoplasty [A] *	0/237 (0%)	0/10 (0%)	1/208 (0.48%)	1/239 (0.42%)
Vascular disorders				
Haematoma [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)

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A Term from vocabulary, MedDRA (18.1)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Cohort 1: SC (SID) Herceptin (Crossover)	Cohort 1: IV Herceptin (Crossover)	Cohort 1: IV Herceptin (Continuation)	Cohort 1: SC (SID) Herceptin (Continuation)	Cohort 1 Overall: SC (SID) and IV Herceptin	Cohort 2: SC (Vial) Herceptin (Crossover)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Total	81/242 (33.47%)	55/241 (22.82%)	46/226 (20.35%)	7/43 (16.28%)	130/244 (53.28%)	107/237 (45.15%)
Cardiac disorders						
Sinus bradycardia [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	0/237 (0%)
Gastrointestinal disorders						
Diarrhoea [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	8/237 (3.38%)
Dyspepsia [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	1/237 (0.42%)
Nausea [A] *	14/242 (5.79%)	6/241 (2.49%)	6/226 (2.65%)	1/43 (2.33%)	22/244 (9.02%)	11/237 (4.64%)
General disorders						
Asthenia [A] *	13/242 (5.37%)	10/241 (4.15%)	9/226 (3.98%)	0/43 (0%)	30/244 (12.3%)	17/237 (7.17%)
Chest pain [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	3/237 (1.27%)

	Cohort 1: SC (SID) Herceptin (Crossover)	Cohort 1: IV Herceptin (Crossover)	Cohort 1: IV Herceptin (Continuation)	Cohort 1: SC (SID) Herceptin (Continuation)	Cohort 1 Overall: SC (SID) and IV Herceptin	Cohort 2: SC (Vial) Herceptin (Crossover)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Fatigue [A] *	8/242 (3.31%)	10/241 (4.15%)	7/226 (3.1%)	0/43 (0%)	23/244 (9.43%)	11/237 (4.64%)
Injection site erythema [A] *	13/242 (5.37%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	13/244 (5.33%)	15/237 (6.33%)
Injection site pain [A] *	12/242 (4.96%)	0/241 (0%)	0/226 (0%)	2/43 (4.65%)	13/244 (5.33%)	20/237 (8.44%)
Injection site reaction [A] *	19/242 (7.85%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	19/244 (7.79%)	0/237 (0%)
Medical device discomfort [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	0/237 (0%)
Infections and infestations						
Nasopharyngitis [A] *	5/242 (2.07%)	7/241 (2.9%)	5/226 (2.21%)	1/43 (2.33%)	16/244 (6.56%)	6/237 (2.53%)
Musculoskeletal and connective tissue disorders						
Arthralgia [A] *	10/242 (4.13%)	15/241 (6.22%)	12/226 (5.31%)	1/43 (2.33%)	33/244 (13.52%)	15/237 (6.33%)
Back pain [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	3/237 (1.27%)
Bone pain [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	1/237 (0.42%)
Myalgia [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	2/237 (0.84%)
Pain in extremity [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	15/237 (6.33%)
Nervous system disorders						
Dizziness [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	7/237 (2.95%)
Headache [A] *	8/242 (3.31%)	6/241 (2.49%)	10/226 (4.42%)	0/43 (0%)	21/244 (8.61%)	12/237 (5.06%)
Respiratory, thoracic and mediastinal disorders						
Cough [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	3/237 (1.27%)
Skin and subcutaneous tissue disorders						
Erythema [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	15/237 (6.33%)
Toxic skin eruption [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	0/237 (0%)

	Cohort 1: SC (SID) Herceptin (Crossover)	Cohort 1: IV Herceptin (Crossover)	Cohort 1: IV Herceptin (Continuation)	Cohort 1: SC (SID) Herceptin (Continuation)	Cohort 1 Overall: SC (SID) and IV Herceptin	Cohort 2: SC (Vial) Herceptin (Crossover)
	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)	Affected/ At Risk (%)
Vascular disorders						
Hot flush [A] *	8/242 (3.31%)	6/241 (2.49%)	3/226 (1.33%)	1/43 (2.33%)	18/244 (7.38%)	14/237 (5.91%)
Hypertension [A] *	7/242 (2.89%)	1/241 (0.41%)	5/226 (2.21%)	1/43 (2.33%)	13/244 (5.33%)	0/237 (0%)
Lymphoedema [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	5/237 (2.11%)
Thrombosis [A] *	0/242 (0%)	0/241 (0%)	0/226 (0%)	0/43 (0%)	0/244 (0%)	0/237 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (18.1)

	Cohort 2: IV Herceptin (Crossover)	Cohort 2: IV Herceptin (Continuation)	Cohort 2: SC (Vial) Herceptin (Continuation)	Cohort 2 Overall: SC (Vial) and IV Herceptin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	76/237 (32.07%)	6/10 (60%)	61/208 (29.33%)	154/239 (64.44%)
Cardiac disorders				
Sinus bradycardia [A] *	0/237 (0%)	1/10 (10%)	0/208 (0%)	1/239 (0.42%)
Gastrointestinal disorders				
Diarrhoea [A] *	9/237 (3.8%)	0/10 (0%)	9/208 (4.33%)	23/239 (9.62%)
Dyspepsia [A] *	2/237 (0.84%)	1/10 (10%)	0/208 (0%)	3/239 (1.26%)
Nausea [A] *	8/237 (3.38%)	0/10 (0%)	3/208 (1.44%)	17/239 (7.11%)
General disorders				
Asthenia [A] *	15/237 (6.33%)	0/10 (0%)	11/208 (5.29%)	36/239 (15.06%)
Chest pain [A] *	2/237 (0.84%)	1/10 (10%)	0/208 (0%)	6/239 (2.51%)
Fatigue [A] *	8/237 (3.38%)	1/10 (10%)	5/208 (2.4%)	21/239 (8.79%)
Injection site erythema [A] *	0/237 (0%)	0/10 (0%)	4/208 (1.92%)	17/239 (7.11%)

	Cohort 2: IV Herceptin (Crossover)	Cohort 2: IV Herceptin (Continuation)	Cohort 2: SC (Vial) Herceptin (Continuation)	Cohort 2 Overall: SC (Vial) and IV Herceptin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Injection site pain [A] *	0/237 (0%)	0/10 (0%)	6/208 (2.88%)	24/239 (10.04%)
Injection site reaction [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Medical device discomfort [A] *	0/237 (0%)	1/10 (10%)	0/208 (0%)	1/239 (0.42%)
Infections and infestations				
Nasopharyngitis [A] *	3/237 (1.27%)	1/10 (10%)	6/208 (2.88%)	13/239 (5.44%)
Musculoskeletal and connective tissue disorders				
Arthralgia [A] *	12/237 (5.06%)	0/10 (0%)	10/208 (4.81%)	33/239 (13.81%)
Back pain [A] *	4/237 (1.69%)	1/10 (10%)	1/208 (0.48%)	7/239 (2.93%)
Bone pain [A] *	1/237 (0.42%)	1/10 (10%)	4/208 (1.92%)	7/239 (2.93%)
Myalgia [A] *	3/237 (1.27%)	1/10 (10%)	4/208 (1.92%)	10/239 (4.18%)
Pain in extremity [A] *	5/237 (2.11%)	0/10 (0%)	2/208 (0.96%)	19/239 (7.95%)
Nervous system disorders				
Dizziness [A] *	2/237 (0.84%)	1/10 (10%)	1/208 (0.48%)	11/239 (4.6%)
Headache [A] *	11/237 (4.64%)	0/10 (0%)	11/208 (5.29%)	29/239 (12.13%)
Respiratory, thoracic and mediastinal disorders				
Cough [A] *	5/237 (2.11%)	0/10 (0%)	6/208 (2.88%)	13/239 (5.44%)
Skin and subcutaneous tissue disorders				
Erythema [A] *	3/237 (1.27%)	0/10 (0%)	6/208 (2.88%)	20/239 (8.37%)
Toxic skin eruption [A] *	0/237 (0%)	1/10 (10%)	0/208 (0%)	1/239 (0.42%)
Vascular disorders				
Hot flush [A] *	11/237 (4.64%)	0/10 (0%)	5/208 (2.4%)	27/239 (11.3%)
Hypertension [A] *	0/237 (0%)	0/10 (0%)	0/208 (0%)	0/239 (0%)
Lymphoedema [A] *	7/237 (2.95%)	0/10 (0%)	2/208 (0.96%)	13/239 (5.44%)

	Cohort 2: IV Herceptin (Crossover)	Cohort 2: IV Herceptin (Continuation)	Cohort 2: SC (Vial) Herceptin (Continuation)	Cohort 2 Overall: SC (Vial) and IV Herceptin
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Thrombosis [A] *	2/237 (0.84%)	1/10 (10%)	0/208 (0%)	2/239 (0.84%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (18.1)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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