ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 09/09/2014

A Study of Herceptin (Trastuzumab) in Women With Metastatic Breast Cancer

This study has been completed.

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT00475670

Purpose

This 2 arm study will assess the efficacy and safety of intravenous Herceptin with or without a taxane for the first line treatment of metastatic breast cancer in women who have relapsed at least 12 months after a minimum of 10 months of (neo)adjuvant treatment with Herceptin for HER2-positive early breast cancer.Patients will receive either Herceptin monotherapy (loading dose of 4mg/kg iv, followed by weekly doses of 2mg/kg iv, or 8mg/kg loading dose followed by 3-weekly doses of 6mg/kg)or Herceptin + a taxane (docetaxel 100mg/m2 iv every 3 weeks, or paclitaxel 175mg/m2 iv every 3 weeks or 75mg/m2 every week). The anticipated time on study treatment is until disease progression, and the target sample size is <100 individuals.

Condition	Intervention	Phase
Breast Cancer	Drug: Trastuzumab Drug: Taxane (docetaxel or paclitaxel)	Phase 2

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Non-Randomized, Safety/Efficacy Study
Official Title: An Open-label Study of the Effect of First-line Herceptin Alone or in Combination With a Taxane on Tumor Response and Disease Progression in Patients With Metastatic Breast Cancer Who Relapsed After Receiving Adjuvant Herceptin for HER2-positive Early Breast Cancer

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Percentage of Participants Achieving Complete Response (CR) or Partial Response (PR) According to the Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.0 Guidelines [Time Frame: Baseline (BL); Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited] [Designated as safety issue: No]

  CR was defined for target lesions (TLs) as the disappearance of all lesions, and for nontarget lesions (NTLs) as the disappearance of all nontarget nonmeasurable lesions. PR was defined for TLs as at least a 30 percent (%) decrease from baseline (BL) in the sum of longest diameter (SLD) of TLs. 95% confidence interval for one-sample binomial using Pearson-Clopper method.

Secondary Outcome Measures:

- Duration of Response - Percentage of Participants With Progressive Disease or Death [Time Frame: BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited] [Designated as safety issue: No]

  Duration of response was defined as the time from first confirmed CR or PR until death or progressive disease (PD). For TLs, PD was defined as at least a 20% increase in the SLD of the TL, taking as reference the smallest SLD recorded since the beginning of treatment or the appearance of one or more new lesions. For NTLs, PD was defined as the appearance of one or more new lesions or unequivocal progression of existing non target non-measurable lesions. Participants were censored at the date of the last tumor assessment.
- Duration of Response [Time Frame: BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited] [Designated as safety issue: No]

  The time, in months, from when the response (CR or PR) was first noted until the date of documented PD, death, or withdrawal, whichever occurred first. Participants were censored at the date of the last tumor assessment.
- Progression-free Survival (PFS) - Percentage of Participants With Progressive Disease [Time Frame: BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited] [Designated as safety issue: No]

  PFS was defined as the time from day of first study drug infusion until death or PD. Participants were censored at the date of the last tumor assessment.
- Progression-Free Survival [Time Frame: BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited] [Designated as safety issue: No]

  The time, in months, from BL to PFS event.
- Percentage of Participants With Treatment Failure [Time Frame: BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited] [Designated as safety issue: No]

  Treatment failure was defined as the time from first study drug infusion to failure. Failure was defined as any of the following: PD, death, withdrawal due to adverse event (AE) or lab abnormality, or refusal of treatment. Participants were censored at the last date recorded in the case report form (CRF) or the date of withdrawal.
- Time to Treatment Failure [Time Frame: BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited] [Designated as safety issue: No]

  The time, in months, from BL to treatment failure.
- Percentage of Participants With Clinical Benefit According to RECIST Guidelines [Time Frame: BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited] [Designated as safety issue: No]

  Clinical benefit was defined as stable disease (SD) for 6 months or longer, or a confirmed overall response of CR or PR. For TLs, SD was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest SLD since the beginning of treatment. For NTLs, SD was synonymous with incomplete response and defined as the persistence of one or more NTLs and/or maintenance of tumor marker level above the normal limits.
- Overall Survival - Percentage of Participants Who Died [Time Frame: BL, Day 1 of Weeks 1, 4, 7, 10, 13, 16, 19, 25, 37, and 5 at the last administration of study treatment, every 24 weeks thereafter until disease progression or death, yearly thereafter up to 2 years after cessation of recruitment] [Designated as safety issue: No]

OS was defined as the time from the date of enrollment to the date of death due to any cause. Participants were censored at the last date recorded in the CRF.

- Overall Survival [Time Frame: BL, Day 1 of Weeks 1, 4, 7, 10, 13, 16, 19, 25, 37, and 52 at the last administration of study treatment, every 24 weeks thereafter until disease progression or death, yearly thereafter up to 2 years after cessation of recruitment] [Designated as safety issue: No]
  The time, in months, from BL to death due to any cause.

Enrollment: 44
Study Start Date: October 2005
Primary Completion Date: June 2012
Study Completion Date: June 2012

Arms	Assigned Interventions
Active Comparator: Trastuzumab Monotherapy Participants received an initial loading dose of 4 milligrams per kilogram (mg/kg) trastuzumab intravenous (i.v.) on Day 1, followed by 2mg/kg i.v. weekly, or an initial loading dose of 8 mg/kg i.v. loading dose on Day 1, followed by 6 mg/kg i.v. every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.	Drug: Trastuzumab 4 mg/kg i.v. loading dose on Day 1, followed by 2 mg/kg i.v. weekly; or 8 mg/kg i.v. loading dose, followed by 6 mg/kg i.v. every 3 weeks until disease progression, unacceptable toxicity, withdrawal or death. Other Names: Herceptin
Experimental: Trastuzumab, Taxane Participant received an initial loading dose of 4 mg/kg trastuzumab i.v. on Day 1, followed by 2mg/kg i.v. weekly, or an initial loading dose of 8 mg/kg i.v. loading dose, followed by 6 mg/kg i.v. every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death; and concomitant taxane, which is either 100 milligrams per square meter (mg/m2) docetaxel i.v. every 3 weeks, or 75 mg/m2 weekly or 175 mg/m2 every 3 weeks paclitaxel for at least 18 weeks, or more at the discretion of the investigator.	Drug: Trastuzumab 4 mg/kg i.v. loading dose on Day 1, followed by 2 mg/kg i.v. weekly; or 8 mg/kg i.v. loading dose, followed by 6 mg/kg i.v. every 3 weeks until disease progression, unacceptable toxicity, withdrawal or death. Other Names: Herceptin Drug: Taxane (docetaxel or paclitaxel) Docetaxel 100 mg/m2 i.v. every 3 weeks, or paclitaxel administered in a dose of 75 mg/m2 i.v. weekly or 175 mg/m2 i.v. every 3 weeks for at least 18 weeks, or more at the discretion of the investigator. Choice of taxane at the discretion of the investigator. Taxane may be administered at the same time, or 24 hours after, administration of trastuzumab. Other Names: Docetaxel Paclitaxel

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Female
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- at least 10 months of Herceptin treatment for HER2-positive early breast cancer;
- metastatic breast cancer >=12 months after discontinuation of Herceptin;
- measurable disease.

Exclusion Criteria:

- previous chemotherapy for metastatic breast cancer;
- brain metastases;
- invasive malignancy other than metastatic breast cancer.

Contacts and Locations

Locations

Australia, Victoria
Geelong, Victoria, Australia, 3220
Austria
Klagenfurt, Austria, 9026
Salzburg, Austria, 5020
Vöcklabruck, Austria, 4840
Wien, Austria, 1090
Belgium
Brussel, Belgium, 1090
Namur, Belgium, 5000
Brazil
Porto Alegre, RS, Brazil, 91350-200
Porto Alegre, RS, Brazil, 90610-000
Canada, Manitoba
Winnipeg, Manitoba, Canada, R2H 2A6
Canada, Ontario
Brampton, Ontario, Canada, L6R 3J7
Oshawa, Ontario, Canada, L1G 2B9
Canada, Quebec
Greenfield Park, Quebec, Canada, J4V 2H1
China
Beijing, China, 100021

Guangzhou, China, 510060
Shanghai, China, 200032
Wuhan, China, 430030

Germany
Berlin, Germany, 12203
Düsseldorf, Germany, 40225
Hamburg, Germany, 20246
Krefeld, Germany, 47805
Köln, Germany, 50931
Lemgo, Germany, 32657
München, Germany, 81675
Tübingen, Germany, 72076

Hungary
Budapest, Hungary, 1031
Budapest, Hungary, 1145
Budapest, Hungary, 1083
Budapest, Hungary, 1122
Kecskemet, Hungary, 6000
Szeged, Hungary, 6701

Italy
Chieti, Italy, 66100
Genova, Italy, 16132
Roma, Italy, 00168
San Giovanni Rotondo, Italy, 71013
Sassari, Italy, 07100

Mexico
Merida, Mexico, 97500

Panama
Panama City, Panama, 83-0669

Poland
Gdansk, Poland, 80-214
Gliwice, Poland, 44-101
Lodz, Poland, 94-306

Russian Federation
Kazan, Russian Federation, 420029
Moscow, Russian Federation, 115478
Saint-Petersburg, Russian Federation, 197758

Spain
Barcelona, Barcelona, Spain, 08035
Barcelona, Barcelona, Spain, 08036
Jaen, Jaen, Spain, 23007
La Coruna, La Coruña, Spain, 15009
Madrid, Madrid, Spain, 28041
Valencia, Valencia, Spain, 46010
Valencia, Valencia, Spain, 46009

Zaragoza, Zaragoza, Spain, 50009

Taiwan

Changhua, Taiwan, 500
Taipei, Taiwan, 00112
Taipei, Taiwan
Taipei, Taiwan, 100
Taoyuan, Taiwan, 333

Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party:	Hoffmann-La Roche
Study ID Numbers:	WO17299
Health Authority:	Australia: Ministry of Health

Study Results

Participant Flow

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 milligrams per kilogram (mg/kg), intravenously (IV), on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/square meter (m^2), IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Overall Study

	Trastuzumab Monotherapy	Trastuzumab, Taxane
Started	3	41
Completed	0 [1]	0

	Trastuzumab Monotherapy	Trastuzumab, Taxane
Not Completed	3	41
Death	0	1
Lack of Efficacy	3	34
Refused treatment	0	2
Failure to Return	0	1
Not Specified	0	3

[1] This cohort was closed prematurely (with only 3 participants) because of enrollment difficulties.

Baseline Characteristics

Analysis Population Description

Full analysis set (FAS) included all enrolled participants who received at least one dose of either trastuzumab or taxane.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 mg/kg, IV, on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/m^2, IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Baseline Measures

	Trastuzumab Monotherapy	Trastuzumab, Taxane	Total
Number of Participants	3	41	44
Age, Continuous [units: years] Median (Full Range)	40 (35 to 58)	54 (31 to 78)	54 (31 to 78)
Gender, Male/Female [units: participants]			
Female	3	41	44

	Trastuzumab Monotherapy	Trastuzumab, Taxane	Total
Male	0	0	0

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants Achieving Complete Response (CR) or Partial Response (PR) According to the Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.0 Guidelines
Measure Description	CR was defined for target lesions (TLs) as the disappearance of all lesions, and for nontarget lesions (NTLs) as the disappearance of all nontarget nonmeasurable lesions. PR was defined for TLs as at least a 30 percent (%) decrease from baseline (BL) in the sum of longest diameter (SLD) of TLs. 95% confidence interval for one-sample binomial using Pearson-Clopper method.
Time Frame	Baseline (BL); Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited
Safety Issue?	No

Analysis Population Description

FAS; Cohort A (trastuzumab monotherapy) was closed prematurely due to enrollment difficulties. Therefore, Cohort A included only 3 participants and none of the data from these 3 participants were analyzed for any of the specified endpoints.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 mg/kg, IV, on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/m^2, IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Measured Values

	Trastuzumab Monotherapy	Trastuzumab, Taxane
Number of Participants Analyzed	0	41
Percentage of Participants Achieving Complete Response (CR) or Partial Response (PR) According to the Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.0 Guidelines		61.0 (48.7 to 80.4)

	Trastuzumab Monotherapy	Trastuzumab, Taxane
[units: percentage of participants] Number (95% Confidence Interval)		

2. Secondary Outcome Measure:

Measure Title	Duration of Response - Percentage of Participants With Progressive Disease or Death
Measure Description	Duration of response was defined as the time from first confirmed CR or PR until death or progressive disease (PD). For TLs, PD was defined as at least a 20% increase in the SLD of the TL, taking as reference the smallest SLD recorded since the beginning of treatment or the appearance of one or more new lesions. For NTLs, PD was defined as the appearance of one or more new lesions or unequivocal progression of existing non target non-measurable lesions. Participants were censored at the date of the last tumor assessment.
Time Frame	BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited
Safety Issue?	No

Analysis Population Description

FAS. Duration of response was assessed in participants with a best overall response of CR or PR. Cohort A (trastuzumab monotherapy) was closed prematurely due to enrollment difficulties. Therefore, Cohort A included only 3 participants and none of the data from these 3 participants were analyzed for any of the specified endpoints.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 mg/kg, IV, on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/m^2, IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Measured Values

	Trastuzumab Monotherapy	Trastuzumab, Taxane
Number of Participants Analyzed	0	25
Duration of Response - Percentage of Participants With Progressive Disease or Death		88.0

	Trastuzumab Monotherapy	Trastuzumab, Taxane
[units: percentage of participants]		

3. Secondary Outcome Measure:

Measure Title	Duration of Response
Measure Description	The time, in months, from when the response (CR or PR) was first noted until the date of documented PD, death, or withdrawal, whichever occurred first. Participants were censored at the date of the last tumor assessment.
Time Frame	BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited
Safety Issue?	No

Analysis Population Description

FAS. Duration of response was assessed in participants with a best overall response of CR or PR. Cohort A (trastuzumab monotherapy) was closed prematurely due to enrollment difficulties. Therefore, Cohort A included only 3 participants and none of the data from these 3 participants were analyzed for any of the specified endpoints.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 mg/kg, IV, on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/m^2, IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Measured Values

	Trastuzumab Monotherapy	Trastuzumab, Taxane
Number of Participants Analyzed	0	25
Duration of Response [units: months] Median (95% Confidence Interval)		8.0 (5 to 15)

4. Secondary Outcome Measure:

Measure Title	Progression-free Survival (PFS) - Percentage of Participants With Progressive Disease
Measure Description	PFS was defined as the time from day of first study drug infusion until death or PD. Participants were censored at the date of the last tumor assessment.
Time Frame	BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited
Safety Issue?	No

Analysis Population Description

FAS; Cohort A (trastuzumab monotherapy) was closed prematurely due to enrollment difficulties. Therefore, Cohort A included only 3 participants and none of the data from these 3 participants were analyzed for any of the specified endpoints.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 mg/kg, IV, on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/m^2, IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Measured Values

	Trastuzumab Monotherapy	Trastuzumab, Taxane
Number of Participants Analyzed	0	41
Progression-free Survival (PFS) - Percentage of Participants With Progressive Disease [units: percentage of participants]		87.8

5. Secondary Outcome Measure:

Measure Title	Progression-Free Survival
Measure Description	The time, in months, from BL to PFS event.
Time Frame	BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited

Safety Issue?	No

Analysis Population Description

FAS; Cohort A (trastuzumab monotherapy) was closed prematurely due to enrollment difficulties. Therefore, Cohort A included only 3 participants and none of the data from these 3 participants were analyzed for any of the specified endpoints.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 mg/kg, IV, on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/m^2, IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Measured Values

	Trastuzumab Monotherapy	Trastuzumab, Taxane
Number of Participants Analyzed	0	41
Progression-Free Survival [units: months] Median (95% Confidence Interval)		8.0 (6 to 11)

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Treatment Failure
Measure Description	Treatment failure was defined as the time from first study drug infusion to failure. Failure was defined as any of the following: PD, death, withdrawal due to adverse event (AE) or lab abnormality, or refusal of treatment. Participants were censored at the last date recorded in the case report form (CRF) or the date of withdrawal.
Time Frame	BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited
Safety Issue?	No

Analysis Population Description

FAS; Cohort A (trastuzumab monotherapy) was closed prematurely due to enrollment difficulties. Therefore, Cohort A included only 3 participants and none of the data from these 3 participants were analyzed for any of the specified endpoints.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 mg/kg, IV, on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/m^2, IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Measured Values

	Trastuzumab Monotherapy	Trastuzumab, Taxane
Number of Participants Analyzed	0	41
Percentage of Participants With Treatment Failure [units: percentage of participants]		95.1

7. Secondary Outcome Measure:

Measure Title	Time to Treatment Failure
Measure Description	The time, in months, from BL to treatment failure.
Time Frame	BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited
Safety Issue?	No

Analysis Population Description

FAS; Cohort A (trastuzumab monotherapy) was closed prematurely due to enrollment difficulties. Therefore, Cohort A included only 3 participants and none of the data from these 3 participants were analyzed for any of the specified endpoints.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 mg/kg, IV, on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.

	Description
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/m^2, IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Measured Values

	Trastuzumab Monotherapy	Trastuzumab, Taxane
Number of Participants Analyzed	0	41
Time to Treatment Failure [units: months] Median (95% Confidence Interval)		8.0 (6 to 11)

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Clinical Benefit According to RECIST Guidelines
Measure Description	Clinical benefit was defined as stable disease (SD) for 6 months or longer, or a confirmed overall response of CR or PR. For TLs, SD was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest SLD since the beginning of treatment. For NTLs, SD was synonymous with incomplete response and defined as the persistence of one or more NTLs and/or maintenance of tumor marker level above the normal limits.
Time Frame	BL, Day 1 of Weeks 7, 13, 19, 25, 37, and 52, at the last administration of study treatment, every 24 weeks thereafter until disease progression for up to 6 months after the last participant was recruited
Safety Issue?	No

Analysis Population Description

FAS; Cohort A (trastuzumab monotherapy) was closed prematurely due to enrollment difficulties. Therefore, Cohort A included only 3 participants and none of the data from these 3 participants were analyzed for any of the specified endpoints.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 mg/kg, IV, on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.

	Description
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/m^2, IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Measured Values

	Trastuzumab Monotherapy	Trastuzumab, Taxane
Number of Participants Analyzed	0	41
Percentage of Participants With Clinical Benefit According to RECIST Guidelines [units: percentage of participants] Number (95% Confidence Interval)		70.7 (54.5 to 83.9)

9. Secondary Outcome Measure:

Measure Title	Overall Survival - Percentage of Participants Who Died
Measure Description	OS was defined as the time from the date of enrollment to the date of death due to any cause. Participants were censored at the last date recorded in the CRF.
Time Frame	BL, Day 1 of Weeks 1, 4, 7, 10, 13, 16, 19, 25, 37, and 5 at the last administration of study treatment, every 24 weeks thereafter until disease progression or death, yearly thereafter up to 2 years after cessation of recruitment
Safety Issue?	No

Analysis Population Description

FAS; Cohort A (trastuzumab monotherapy) was closed prematurely due to enrollment difficulties. Therefore, Cohort A included only 3 participants and none of the data from these 3 participants were analyzed for any of the specified endpoints.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 mg/kg, IV, on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.

	Description
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/m^2, IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Measured Values

	Trastuzumab Monotherapy	Trastuzumab, Taxane
Number of Participants Analyzed	0	41
Overall Survival - Percentage of Participants Who Died [units: percentage of participants]		63.4

10. Secondary Outcome Measure:

Measure Title	Overall Survival
Measure Description	The time, in months, from BL to death due to any cause.
Time Frame	BL, Day 1 of Weeks 1, 4, 7, 10, 13, 16, 19, 25, 37, and 52 at the last administration of study treatment, every 24 weeks thereafter until disease progression or death, yearly thereafter up to 2 years after cessation of recruitment
Safety Issue?	No

Analysis Population Description

FAS; Cohort A (trastuzumab monotherapy) was closed prematurely due to enrollment difficulties. Therefore, Cohort A included only 3 participants and none of the data from these 3 participants were analyzed for any of the specified endpoints.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 mg/kg, IV, on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/m^2, IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Measured Values

	Trastuzumab Monotherapy	Trastuzumab, Taxane
Number of Participants Analyzed	0	41
Overall Survival [units: months] Median (95% Confidence Interval)		25.0 (16 to 33)

Reported Adverse Events

Time Frame	Adverse events and serious adverse events were recorded from study start to 28 days after the last dose of study drug. Serious adverse events that were related to study medication or were cardiac are reported until 2 years after enrollment.
Additional Description	The safety analysis population included all participants who received at least 1 dose of either trastuzumab or taxane.

Reporting Groups

	Description
Trastuzumab Monotherapy	Participants received either an initial loading dose of trastuzumab 4 mg/kg, IV, on Day 1, followed by 2 mg/kg, IV, once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV once every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death.
Trastuzumab, Taxane	Participants received either an initial loading dose of trastuzumab 4 mg/kg IV on Day 1, followed by 2 mg/kg IV once per week, or an initial loading dose of 8 mg/kg IV on Day 1, followed by 6 mg/kg IV every 3 weeks, until disease progression, unacceptable toxicity, withdrawal or death. Participants also received one of the following taxanes (at the investigator's discretion) for at least 18 weeks: docetaxel 100 mg/m^2, IV, once every 3 weeks, OR, paclitaxel 75 mg/m^2, IV, once per week, OR, paclitaxel 175 mg/m^2, IV, once every 3 weeks.

Serious Adverse Events

	Trastuzumab Monotherapy	Trastuzumab, Taxane
	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/3 (0%)	6/41 (14.63%)
Blood and lymphatic system disorders		
Febrile Neutropenia [A] *	0/3 (0%)	1/41 (2.44%)

	Trastuzumab Monotherapy	Trastuzumab, Taxane
	Affected/At Risk (%)	Affected/At Risk (%)
Neutropenia [A] *	0/3 (0%)	1/41 (2.44%)
General disorders		
Sudden Death [A] *	0/3 (0%)	1/41 (2.44%)
Infections and infestations		
Bacterial Infection [A] *	0/3 (0%)	1/41 (2.44%)
Bronchitis [A] *	0/3 (0%)	1/41 (2.44%)
Sepsis [A] *	0/3 (0%)	1/41 (2.44%)
Vascular disorders		
Lymphoedema [A] *	0/3 (0%)	1/41 (2.44%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (15.0)

Other Adverse Events

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

	Trastuzumab Monotherapy	Trastuzumab, Taxane
	Affected/At Risk (%)	Affected/At Risk (%)
Total	3/3 (100%)	36/41 (87.8%)
Blood and lymphatic system disorders		
Neutropenia [A] *	0/3 (0%)	5/41 (12.2%)
Eye disorders		
Lacrimation increased [A] *	0/3 (0%)	4/41 (9.76%)
Gastrointestinal disorders		
Abdominal pain [A] *	0/3 (0%)	4/41 (9.76%)
Diarrhoea [A] *	0/3 (0%)	13/41 (31.71%)
Dyspepsia [A] *	0/3 (0%)	3/41 (7.32%)

	Trastuzumab Monotherapy	Trastuzumab, Taxane
	Affected/At Risk (%)	Affected/At Risk (%)
Nausea [A] *	0/3 (0%)	6/41 (14.63%)
Stomatitis [A] *	0/3 (0%)	4/41 (9.76%)
Vomiting [A] *	0/3 (0%)	5/41 (12.2%)
General disorders		
Asthenia [A] *	0/3 (0%)	6/41 (14.63%)
Fatigue [A] *	0/3 (0%)	10/41 (24.39%)
Oedema peripheral [A] *	1/3 (33.33%)	7/41 (17.07%)
Pyrexia [A] *	1/3 (33.33%)	6/41 (14.63%)
Infections and infestations		
Bronchitis [A] *	0/3 (0%)	4/41 (9.76%)
Nasopharyngitis [A] *	0/3 (0%)	3/41 (7.32%)
Urinary tract infection [A] *	1/3 (33.33%)	0/41 (0%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	0/3 (0%)	4/41 (9.76%)
Back pain [A] *	1/3 (33.33%)	4/41 (9.76%)
Musculoskeletal pain [A] *	1/3 (33.33%)	3/41 (7.32%)
Myalgia [A] *	0/3 (0%)	6/41 (14.63%)
Nervous system disorders		
Headache [A] *	1/3 (33.33%)	3/41 (7.32%)
Neuropathy peripheral [A] *	0/3 (0%)	3/41 (7.32%)
Paraesthesia [A] *	0/3 (0%)	4/41 (9.76%)
Peripheral sensory neuropathy [A] *	0/3 (0%)	5/41 (12.2%)
Respiratory, thoracic and mediastinal disorders		

	Trastuzumab Monotherapy	Trastuzumab, Taxane
	Affected/At Risk (%)	Affected/At Risk (%)
Cough [A] *	1/3 (33.33%)	0/41 (0%)
Dyspnoea [A] *	1/3 (33.33%)	4/41 (9.76%)
Skin and subcutaneous tissue disorders		
Alopecia [A] *	0/3 (0%)	13/41 (31.71%)
Dermatitis allergic [A] *	0/3 (0%)	3/41 (7.32%)
Nail disorder [A] *	0/3 (0%)	7/41 (17.07%)
Rash [A] *	0/3 (0%)	6/41 (14.63%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (15.0)

Limitations and Caveats

Cohort A (trastuzumab monotherapy) was closed prematurely due to enrollment difficulties. Therefore, Cohort A included only 3 participants.

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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