ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 11/25/2014

A Study to Evaluate the Effect of the Combination of Pertuzumab With Carboplatin-Based Standard Chemotherapy in Patients With Recurrent Ovarian Cancer

This study has been completed.

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT02004093

Purpose

This study will evaluate the efficacy and safety of pertuzumab in combination with carboplatin-based standard chemotherapy in patients with platinum-sensitive recurrent ovarian cancer. The anticipated time on study treatment is 3-12 months.

Condition	Intervention	Phase
Ovarian Cancer	Drug: pertuzumab Drug: paclitaxel Drug: gemcitabine Drug: carboplatin	Phase 2

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study
Official Title: A Randomized, Open-label Study of the Effect of Omnitarg in Combination With Carboplatin-based Chemotherapy Versus Carboplatin-based Therapy Alone on Treatment Response in Patients With Platinum-sensitive Recurrent Ovarian Cancer

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Percentage of Participants With Disease Progression or Death [Time Frame: Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until disease progression up to 104 weeks] [Designated as safety issue: No]
  Disease progression was assessed according to RECIST (Response Evaluation Criteria In Solid Tumors), for participants with measurable disease, or by changes in CA 125 (Cancer Antigen 125) according to GCIG (Gynecologic Cancer Inter Group) for all participants. Participants who did not progress or died while being followed were censored at the time of the last valid tumor assessment or valid CA 125 assessment.
- Progression-Free Survival [Time Frame: Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until disease progression up to 104 weeks] [Designated as safety issue: No]
  Progression-free survival was defined as the time from first administration of study drug (Study Day 1) to documented disease progression or death, whichever occurred earlier. Disease progression was assessed according to RECIST, for participants with measurable disease, or by changes in CA 125 according to GCIG for all participants. Participants who did not progress or died while being followed were censored at the time of the last valid tumor assessment or valid CA 125 assessment.
- Kaplan-Meier Probability of No Disease or Progression at 1 Year [Time Frame: 1 year] [Designated as safety issue: No]
  The probability of being event free (no disease progression or death events) at 1 year in participants remaining at risk.

Secondary Outcome Measures:

- Percentage of Participants With a Best Overall Confirmed Response Based on Combined CA 125 and RECIST Measurements [Time Frame: Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until disease progression up to 104 weeks] [Designated as safety issue: No]
  Response by tumor measurement occurred if there was documented and confirmed complete response (CR) or partial response (PR). For all participants, response was assessed by both the RECIST and by CA 125 levels, according to whether the participant had measurable or non-measurable disease at baseline. Response according to CA 125 levels was defined as at least a 50% reduction from baseline. The decrease had to be confirmed and maintained for at least 28 days. The confirmatory sample must have been less than or equal to the previous sample (within an assay variability of 10%). For overall response, the response categories were "response", "stable disease" and "progressive disease". Stable disease included 1) stable disease as defined by RECIST for solid tumors and 2) CA 125 levels that had not met the definition of "response" or "progressive disease".
- Duration of Response [Time Frame: Day 15 of Cycles 2, 4, 6, and Day 15 of all Cycles from Cycle 7 to 17 until disease progression up to 104 weeks] [Designated as safety issue: No]
  For participants who achieved a response, the duration of response was defined as the interval between initial documentation of response to the first documentation of disease progression or death. Participants who responded and did not progress or die while on study or while being followed were censored at the last valid tumor or CA 125 measurement.
- Kaplan-Meier Probability of Maintaining a Response to at Least 1 Year [Time Frame: 1 year] [Designated as safety issue: No]
- Percentage of Participants With Disease Progression [Time Frame: Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until disease progression] [Designated as safety issue: No]
  Disease progression was assessed according to RECIST, for participants with measurable disease, or by changes in CA 125 according to GCIG for all participants. Participants who did not progress while being followed were censored at the time of the last valid tumor assessment or valid CA 125 assessment.
- Time to Progressive Disease [Time Frame: Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until disease progression] [Designated as safety issue: No]
  The time to progressive disease is the interval of time from date of first dose of study medication to date of first documentation of progressive disease by either RECIST or CA 125 criteria. Participants who never progressed while being followed were censored at the last valid tumor measurement or CA 125 measurement.
- Kaplan-Meier Probability of Being Progression Free at 1 Year [Time Frame: 1 year] [Designated as safety issue: No]
- Time To Response [Time Frame: Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until 2 years after last dose of treatment] [Designated as safety issue: No]
  Time to response was the date of first dose of study medication to the date of the first documentation of response, according to CA 125 criteria for all participants or response according to RECIST criteria for participants with measurable disease. If response was evaluable by both criteria, then the date of response was for the earlier of the two events.

- Percentage of Participants Who Died [Time Frame: Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until 2 years after last dose of treatment] [Designated as safety issue: No]
- Overall Survival [Time Frame: Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until 2 years after last dose of treatment] [Designated as safety issue: No]
  Survival was the interval of time from date of first dose of study medication to date of death at any time. Participants who had not died were censored at the date of last contact when they were known to be alive.
- Kaplan-Meier Probability of Being Alive at 1 Year [Time Frame: 1 year] [Designated as safety issue: No]

Enrollment: 149
Study Start Date: December 2005
Primary Completion Date: September 2008
Study Completion Date: September 2008

Arms	Assigned Interventions
Experimental: Chemotherapy + Pertuzumab	Drug: pertuzumab Loading dose of 840 mg IV, followed by 420 mg IV every 3 weeks Drug: paclitaxel 175 mg/m2 IV every 3 weeks for 6 cycles Drug: gemcitabine 1000 mg/m2 IV Day 1 and 8 of each cycle for 6 cycles Drug: carboplatin Target AUC of 5 following paclitaxel or AUC of 4 following gemcitabine IV every 3 weeks for 6 cycles
Active Comparator: Chemotherapy	Drug: paclitaxel 175 mg/m2 IV every 3 weeks for 6 cycles Drug: gemcitabine 1000 mg/m2 IV Day 1 and 8 of each cycle for 6 cycles Drug: carboplatin Target AUC of 5 following paclitaxel or AUC of 4 following gemcitabine IV every 3 weeks for 6 cycles

Eligibility

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

Criteria

Inclusion Criteria:

- histologically confirmed ovarian, primary peritoneal, or fallopian tube cancer;
- only 1 previous regimen, which must be platinum-based;
- platinum-sensitive disease which is defined by a progression-free interval of greater than 6 months after completion of platinum-based chemotherapy.

Exclusion Criteria:

- previous radiotherapy;
- previous treatment with an anti-cancer vaccine or any targeted therapy;
- major surgery or traumatic injury within 4 weeks of study;
- history or evidence of central nervous system metastases.

Contacts and Locations

Locations

Belgium
- Bruxelles, Belgium, 1000
- Leuven, Belgium, 3000
- Wilrijk, Belgium, 2610

Canada, Alberta
- Calgary, Alberta, Canada, T2N 4N2

Canada, British Columbia
- Kelowna, British Columbia, Canada, V1Y 5L3
- Vancouver, British Columbia, Canada, V5Z 4E6

Hungary
- Budapest, Hungary, 1122
- Debrecen, Hungary, 4032
- Gyor, Hungary, 9024

Italy
- Parma, Emilia-Romagna, Italy, 43100
- Milano, Lombardia, Italy, 20133

Netherlands
- Amsterdam, Netherlands, 1081 HV
- Amsterdam, Netherlands, 1066 CX

Poland
- Poznan, Poland, 60-535
- Warszawa, Poland, 02-781

Russian Federation
- Kazan, Russian Federation, 420029
- Moscow, Russian Federation, 117837
- Moscow, Russian Federation, 115478
- Moscow, Russian Federation, 105203
- Moscow, Russian Federation, 143423
- Moscow, Russian Federation, 125284

Saint-Petersburg, Russian Federation, 197022
St Petersburg, Russian Federation, 197758
Tomsk, Russian Federation, 634028

Spain

Barcelona, Barcelona, Spain, 08035
Barcelona, Barcelona, Spain, 08036
Madrid, Madrid, Spain, 28041
Valencia, Valencia, Spain, 46009

United Kingdom

Birmingham, United Kingdom, B18 7QH
London, United Kingdom, W12 OHS
Manchester, United Kingdom, M20 4BX
Plymouth, United Kingdom, PL6 8DH
Sutton, United Kingdom, SM2 5PT
Yeovil, United Kingdom, BA21 4AT

Investigators

Study Chair:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party:	Hoffmann-La Roche
Study ID Numbers:	BO17931
Health Authority:	Belgium: Ministry of Social Affairs, Public Health and the Environment

Study Results

Participant Flow

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 milligrams (mg) intravenously (IV) on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/square meters (m^2) IV on Day 1 and carboplatin target area under the curve (AUC) 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

	Description
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Overall Study

	Chemotherapy + Pertuzumab	Chemotherapy
Started	75 [1]	74
Completed	1	1
Not Completed	74	73
Death	2	1
Lack of Efficacy	66	62
Protocol Violation	0	1
Lost to Follow-up	0	1
Withdrawal by Subject	3	7
Not specified	3	1

[1] Includes 1 participant who was randomized to chemotherapy group but received pertuzumab+chemotherapy

Baseline Characteristics

Analysis Population Description

All participants who received randomized treatment (All Treated Population, for Efficacy Analyses); 1 participant was randomized to the chemotherapy arm but received pertuzumab+chemotherapy and is thus included in this arm for all analyses.

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER: 1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

	Description
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Baseline Measures

	Chemotherapy + Pertuzumab	Chemotherapy	Total
Number of Participants	74	75	149
Age, Continuous [units: years] Mean (Standard Deviation)	58.1 (10.16)	55.3 (11.41)	56.7 (10.86)
Gender, Male/Female [units: participants]			
Female	74	75	149
Male	0	0	0

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Disease Progression or Death
Measure Description	Disease progression was assessed according to RECIST (Response Evaluation Criteria In Solid Tumors), for participants with measurable disease, or by changes in CA 125 (Cancer Antigen 125) according to GCIG (Gynecologic Cancer Inter Group) for all participants. Participants who did not progress or died while being followed were censored at the time of the last valid tumor assessment or valid CA 125 assessment.
Time Frame	Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until disease progression up to 104 weeks
Safety Issue?	No

Analysis Population Description

All treated participants who received Randomized Treatment (All Treated Population, for Efficacy Analyses) were included in analysis.

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	74	75
Percentage of Participants With Disease Progression or Death [units: percentage of participants]	87.8	80.0

2. Primary Outcome Measure:

Measure Title	Progression-Free Survival
Measure Description	Progression-free survival was defined as the time from first administration of study drug (Study Day 1) to documented disease progression or death, whichever occurred earlier. Disease progression was assessed according to RECIST, for participants with measurable disease, or by changes in CA 125 according to GCIG for all participants. Participants who did not progress or died while being followed were censored at the time of the last valid tumor assessment or valid CA 125 assessment.
Time Frame	Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until disease progression up to 104 weeks
Safety Issue?	No

Analysis Population Description

All treated patients who received Randomized Treatment (All Treated Population, for Efficacy Analyses) were included in analysis.

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	74	75
Progression-Free Survival [units: weeks] Median (Full Range)	34.1 (31 to 38)	40.0 (33 to 43)

Statistical Analysis 1 for Progression-Free Survival

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3967
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Statistical Analysis 2 for Progression-Free Survival

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4552
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

Statistical Analysis 3 for Progression-Free Survival

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3972
	Comments	p-value resulting from Wald test of null hypothesis that the hazard ratio equals (=) 1
	Method	Other [Wald test]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.17
	Confidence Interval	(2-Sided) 80% 0.92 to 1.49
	Estimation Comments	[Not specified]

3. Primary Outcome Measure:

Measure Title	Kaplan-Meier Probability of No Disease or Progression at 1 Year
Measure Description	The probability of being event free (no disease progression or death events) at 1 year in participants remaining at risk.
Time Frame	1 year
Safety Issue?	No

Analysis Population Description

All treated patients who received Randomized Treatment (All Treated Population, for Efficacy Analyses) were included in analysis. 17 and 12 participants in the chemotherapy + pertuzumab and chemotherapy treatment groups, respectively, remained at risk.

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	74	75
Kaplan-Meier Probability of No Disease or Progression at 1 Year [units: percent]	24	21

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Best Overall Confirmed Response Based on Combined CA 125 and RECIST Measurements
Measure Description	Response by tumor measurement occurred if there was documented and confirmed complete response (CR) or partial response (PR). For all participants, response was assessed by both the RECIST and by CA 125 levels, according to whether the participant had measurable or non-measurable disease at baseline. Response according to CA 125 levels was defined as at least a 50% reduction from baseline. The decrease had to be confirmed and maintained for at least 28 days. The confirmatory sample must have been less than or equal to the previous sample (within an assay variability of 10%). For overall response, the response categories were “response”, “stable disease” and “progressive disease”. Stable disease included 1) stable disease as defined by RECIST for solid tumors and 2) CA 125 levels that had not met the definition of “response” or “progressive disease”.
Time Frame	Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until disease progression up to 104 weeks

Safety Issue?	No

Analysis Population Description

All treated patients who received Randomized Treatment (All Treated Population, for Efficacy Analyses) were included in analysis.

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	74	75
Percentage of Participants With a Best Overall Confirmed Response Based on Combined CA 125 and RECIST Measurements [units: percentage of participants]	74.3	68.0

Statistical Analysis 1 for Percentage of Participants With a Best Overall Confirmed Response Based on Combined CA 125 and RECIST Measurements

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3943
	Comments	[Not specified]
	Method	Chi-squared

	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Difference in Response Rates]
	Estimated Value	6.32
	Confidence Interval	(2-Sided) 80% -3.9 to 16.6
	Estimation Comments	[Not specified]

Statistical Analysis 2 for Percentage of Participants With a Best Overall Confirmed Response Based on Combined CA 125 and RECIST Measurements

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Odds Ratio (OR)
	Estimated Value	1.36
	Confidence Interval	(2-Sided) 80% 0.86 to 2.17
	Estimation Comments	approximate 80% confidence interval (CI) for difference of two rates using Hauck-Anderson method

5. Secondary Outcome Measure:

Measure Title	Duration of Response
Measure Description	For participants who achieved a response, the duration of response was defined as the interval between initial documentation of response to the first documentation of disease progression or death. Participants who responded and did not progress or die while on study or while being followed were censored at the last valid tumor or CA 125 measurement.
Time Frame	Day 15 of Cycles 2, 4, 6, and Day 15 of all Cycles from Cycle 7 to 17 until disease progression up to 104 weeks
Safety Issue?	No

Analysis Population Description

Only participants with a response were included in the analysis; 8 participants and 13 participants were censored in the chemotherapy + pertuzumab and chemotherapy only treatment groups, respectively.

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles.Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	47	38
Duration of Response [units: weeks] Median (Inter-Quartile Range)	28.7 (22 to 48)	37.0 (25 to 43)

Statistical Analysis 1 for Duration of Response

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3655
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Statistical Analysis 2 for Duration of Response

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.1319
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

Statistical Analysis 3 for Duration of Response

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3679
	Comments	[Not specified]
	Method	Other [Wald test]
	Comments	p-value resulting from Wald test of null hypothesis that the hazard ratio=1

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.22
	Confidence Interval	(2-Sided) 80% 0.92 to 1.61
	Estimation Comments	[Not specified]

6. Secondary Outcome Measure:

Measure Title	Kaplan-Meier Probability of Maintaining a Response to at Least 1 Year
Measure Description	
Time Frame	1 year
Safety Issue?	No

Analysis Population Description

All treated patients who received Randomized Treatment (All Treated Population, for Efficacy Analyses) were included in analysis. 7 and 5 participants in the chemotherapy + pertuzumab and chemotherapy treatment groups, respectively, remained at risk.

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER: 1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	55	51
Kaplan-Meier Probability of Maintaining a Response to at Least 1 Year [units: percent]	18	18

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Disease Progression
Measure Description	Disease progression was assessed according to RECIST, for participants with measurable disease, or by changes in CA 125 according to GCIG for all participants. Participants who did not progress while being followed were censored at the time of the last valid tumor assessment or valid CA 125 assessment.
Time Frame	Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until disease progression
Safety Issue?	No

Analysis Population Description

All treated participants were included in analysis

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	74	75
Percentage of Participants With Disease Progression [units: percentage of participants]	83.8	76.0

8. Secondary Outcome Measure:

Measure Title	Time to Progressive Disease
Measure Description	The time to progressive disease is the interval of time from date of first dose of study medication to date of first documentation of progressive disease by either RECIST or CA 125 criteria. Participants who never progressed while being followed were censored at the last valid tumor measurement or CA 125 measurement.
Time Frame	Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until disease progression
Safety Issue?	No

Analysis Population Description

All treated patients with an event (disease progression) were included in analysis

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	62	57
Time to Progressive Disease [units: weeks] Median (Inter-Quartile Range)	34.3 (27 to 48)	37.3 (29 to 47)

Statistical Analysis 1 for Time to Progressive Disease

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8129
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Statistical Analysis 2 for Time to Progressive Disease

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.6920
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

Statistical Analysis 3 for Time to Progressive Disease

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8137
	Comments	[Not specified]
	Method	Other [Wald test]
	Comments	p-value resulting from Wald test of null hypothesis that the hazard ratio=1

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.04
	Confidence Interval	(2-Sided) 80% 0.82 to 1.32
	Estimation Comments	[Not specified]

9. Secondary Outcome Measure:

Measure Title	Kaplan-Meier Probability of Being Progression Free at 1 Year
Measure Description	
Time Frame	1 year
Safety Issue?	No

Analysis Population Description

All treated patients who received Randomized Treatment (All Treated Population, for Efficacy Analyses) were included in analysis. 16 and 10 participants in the chemotherapy + pertuzumab and chemotherapy treatment groups, respectively, remained at risk.

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	62	57
Kaplan-Meier Probability of Being Progression Free at 1 Year [units: percent]	24	19

10. Secondary Outcome Measure:

Measure Title	Time To Response
Measure Description	Time to response was the date of first dose of study medication to the date of the first documentation of response, according to CA 125 criteria for all participants or response according to RECIST criteria for participants with measurable disease. If response was evaluable by both criteria, then the date of response was for the earlier of the two events.
Time Frame	Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until 2 years after last dose of treatment
Safety Issue?	No

Analysis Population Description

Only participants with a response were included in the analysis.

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen17 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	55	51
Time To Response [units: weeks] Median (Inter-Quartile Range)	6.0 (5 to 17)	6.3 (5 to 15)

Statistical Analysis 1 for Time To Response

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5726
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Statistical Analysis 2 for Time To Response

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.3903
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

Statistical Analysis 3 for Time To Response

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5870
	Comments	[Not specified]
	Method	Other [Wald test]
	Comments	p-value resulting from Wald test of null hypothesis that the hazard ratio=1

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.11
	Confidence Interval	(2-Sided) 80% 0.87 to 1.43
	Estimation Comments	[Not specified]

11. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Died
Measure Description	
Time Frame	Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until 2 years after last dose of treatment
Safety Issue?	No

Analysis Population Description
All treated participants were included in analysis

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	74	75
Percentage of Participants Who Died [units: percentage of participants]	45.9	41.3

12. Secondary Outcome Measure:

Measure Title	Overall Survival
Measure Description	Survival was the interval of time from date of first dose of study medication to date of death at any time. Participants who had not died were censored at the date of last contact when they were known to be alive.
Time Frame	Screening and Day 15 of Cycles 2, 4, 6, and Day 15 of all cycles from Cycle 7 to 17 until 2 years after last dose of treatment
Safety Issue?	No

Analysis Population Description
All treated participants were included in analysis

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	74	75
Overall Survival [units: months] Median (Full Range)	28.2 (1 to 52)	NA (1 to 34) [1]

[1] Given the duration of follow-up at time of data analysis the median had not been reached and could not be calculated (at least 50% of patients had not died).

Statistical Analysis 1 for Overall Survival

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9261
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Statistical Analysis 2 for Overall Survival

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.8591
	Comments	[Not specified]
	Method	Wilcoxon (Mann-Whitney)
	Comments	[Not specified]

Statistical Analysis 3 for Overall Survival

Statistical Analysis Overview	Comparison Groups	Chemotherapy + Pertuzumab, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.9262
	Comments	p-value resulting from Wald test of null hypothesis that the hazard ratio=1
	Method	Other [Wald test]
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.02
	Confidence Interval	(2-Sided) 80% 0.74 to 1.41
	Estimation Comments	[Not specified]

13. Secondary Outcome Measure:

Measure Title	Kaplan-Meier Probability of Being Alive at 1 Year
Measure Description	

Time Frame	1 year
Safety Issue?	No

Analysis Population Description

All treated patients who received Randomized Treatment (All Treated Population, for Efficacy Analyses) were included in analysis.

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received pertuzumab for a total of seventeen 3-week cycles and chemotherapy for a total of six 3-week cycles. Pertuzumab: Participants received pertuzumab 840 mg IV on Day 1 of cycle 1 and 420 mg IV on Day 1 of cycles 2 to 17; Chemotherapy consisted of EITHER:1) paclitaxel 175 mg/m^2 IV on Day 1 and carboplatin target AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.
Chemotherapy	Participants received chemotherapy with EITHER: 1) paclitaxel 175 mg/m^2 on Day 1 and carboplatin AUC 5, IV, on Day 1 followed by 2 weeks off OR 2) gemcitabine 1000 mg/m^2, IV, on Days 1 and 8 (with carboplatin target AUC of 4, IV on Day 1 only) followed by 1 week off.

Measured Values

	Chemotherapy + Pertuzumab	Chemotherapy
Number of Participants Analyzed	64	61
Kaplan-Meier Probability of Being Alive at 1 Year [units: percent]	88	85

Reported Adverse Events

Time Frame	Adverse events were collected from the date of randomization until 28 days after the last dose of the pertuzumab and/ or standard chemotherapy and continuously until end of study.
Additional Description	[Not specified]

Reporting Groups

	Description
Chemotherapy + Pertuzumab	Participants received loading dose of 840mg IV Pertuzumab, followed by 420 mg IV every 3 weeks (for a total of 17 cycles), along with chemotherapy with either Paclitaxel or Gemcitabine. Paclitaxel dosage was 175 mg/ m2 IV every 3 weeks for 6 cycles, followed by Carboplatin AUC of 5; Gemcitabine dosage was 1000 mg/m2 IV on day 1 and 8 of each cycle for 6 cycles followed by Carboplatin AUC of 4, IV every 3 weeks for 6 cycles.
Chemotherapy	Participants received chemotherapy with either Paclitaxel or Gemcitabine. Paclitaxel dosage was 175 mg/m2 IV every 3 weeks for 6 cycles followed by Carboplatin AUC of 5; Gemcitabine dosage was 1000 mg/ m2 IV on day 1 and 8 of each cycle for 6 cycles followed by Carboplatin AUC of 4, IV every 3 weeks for 6 cycles.

Serious Adverse Events

	Chemotherapy + Pertuzumab	Chemotherapy
	Affected/At Risk (%)	Affected/At Risk (%)
Total	20/75 (26.67%)	12/74 (16.22%)
Blood and lymphatic system disorders		
Anaemia [A] †	0/75 (0%)	1/74 (1.35%)
Febrile neutropenia [A] †	0/75 (0%)	3/74 (4.05%)
Cardiac disorders		
Cardiac failure congestive [A] †	1/75 (1.33%)	0/74 (0%)
Left ventricular dysfunction [A] †	1/75 (1.33%)	0/74 (0%)
Gastrointestinal disorders		
Abdominal pain [A] †	2/75 (2.67%)	1/74 (1.35%)
Ascites [A] †	1/75 (1.33%)	1/74 (1.35%)
Constipation [A] †	0/75 (0%)	1/74 (1.35%)
Diarrhoea [A] †	2/75 (2.67%)	0/74 (0%)
Gastrointestinal haemorrhage [A] †	1/75 (1.33%)	0/74 (0%)
Ileus paralytic [A] †	1/75 (1.33%)	0/74 (0%)
Intestinal obstruction [A] †	2/75 (2.67%)	0/74 (0%)
Large intesting perforation [A] †	0/75 (0%)	1/74 (1.35%)

	Chemotherapy + Pertuzumab	Chemotherapy
	Affected/At Risk (%)	Affected/At Risk (%)
Vomiting [A] †	2/75 (2.67%)	0/74 (0%)
General disorders		
Local swelling [A] †	1/75 (1.33%)	0/74 (0%)
Obstruction [A] †	0/75 (0%)	1/74 (1.35%)
Pyrexia [A] †	2/75 (2.67%)	0/74 (0%)
Hepatobiliary disorders		
Hepatic lesion [A] †	1/75 (1.33%)	0/74 (0%)
Immune system disorders		
Drug hypersensitivity [A] †	4/75 (5.33%)	0/74 (0%)
Infections and infestations		
Appendicitis [A] †	0/75 (0%)	1/74 (1.35%)
Cystitis [A] †	1/75 (1.33%)	0/74 (0%)
Lower respiratory tract infection [A] †	1/75 (1.33%)	0/74 (0%)
Pneumonia [A] †	1/75 (1.33%)	0/74 (0%)
Sinusitis [A] †	0/75 (0%)	1/74 (1.35%)
Investigations		
Blood glucose increased [A] †	1/75 (1.33%)	0/74 (0%)
Metabolism and nutrition disorders		
Dehydration [A] †	0/75 (0%)	1/74 (1.35%)
Nervous system disorders		
Neuropathy peripheral [A] †	1/75 (1.33%)	0/74 (0%)
Syncope [A] †	1/75 (1.33%)	0/74 (0%)
Respiratory, thoracic and mediastinal disorders		

	Chemotherapy + Pertuzumab	Chemotherapy
	Affected/At Risk (%)	Affected/At Risk (%)
Diaphragmatic hernia [A] †	1/75 (1.33%)	0/74 (0%)
Epistaxis [A] †	1/75 (1.33%)	0/74 (0%)
Pulmonary embolism [A] †	1/75 (1.33%)	1/74 (1.35%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 13.1

Other Adverse Events

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

	Chemotherapy + Pertuzumab	Chemotherapy
	Affected/At Risk (%)	Affected/At Risk (%)
Total	72/75 (96%)	68/74 (91.89%)
Blood and lymphatic system disorders		
Anaemia [A] †	19/75 (25.33%)	21/74 (28.38%)
Leukopenia [A] †	9/75 (12%)	12/74 (16.22%)
Neutropenia [A] †	36/75 (48%)	43/74 (58.11%)
Thrombocytopenia [A] †	11/75 (14.67%)	18/74 (24.32%)
Gastrointestinal disorders		
Abdominal distension [A] †	1/75 (1.33%)	4/74 (5.41%)
Abdominal pain [A] †	18/75 (24%)	14/74 (18.92%)
Abdominal pain lower [A] †	4/75 (5.33%)	0/74 (0%)
Abdominal pain upper [A] †	5/75 (6.67%)	2/74 (2.7%)
Constipation [A] †	20/75 (26.67%)	22/74 (29.73%)
Diarrhoea [A] †	44/75 (58.67%)	14/74 (18.92%)
Dyspepsia [A] †	9/75 (12%)	6/74 (8.11%)
Hemorrhoids [B] †	6/75 (8%)	1/74 (1.35%)

	Chemotherapy + Pertuzumab	Chemotherapy
	Affected/At Risk (%)	Affected/At Risk (%)
Nausea [A] †	44/75 (58.67%)	33/74 (44.59%)
Stomatitis [A] †	10/75 (13.33%)	3/74 (4.05%)
Vomiting [A] †	24/75 (32%)	22/74 (29.73%)
General disorders		
Asthenia [A] †	9/75 (12%)	10/74 (13.51%)
Chest pain [A] †	5/75 (6.67%)	1/74 (1.35%)
Fatigue [A] †	30/75 (40%)	27/74 (36.49%)
Mucosal inflammation [A] †	7/75 (9.33%)	1/74 (1.35%)
Oedema peripheral [A] †	4/75 (5.33%)	6/74 (8.11%)
Pyrexia [A] †	5/75 (6.67%)	3/74 (4.05%)
Immune system disorders		
Drug hypersensitivity [A] †	11/75 (14.67%)	13/74 (17.57%)
Infections and infestations		
Cystitis [A] †	7/75 (9.33%)	0/74 (0%)
Nasopharyngitis [A] †	5/75 (6.67%)	2/74 (2.7%)
Urinary tract infection [A] †	6/75 (8%)	2/74 (2.7%)
Metabolism and nutrition disorders		
Decreased appetite [A] †	19/75 (25.33%)	4/74 (5.41%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	11/75 (14.67%)	4/74 (5.41%)
Back pain [A] †	6/75 (8%)	3/74 (4.05%)
Bone pain [A] †	5/75 (6.67%)	7/74 (9.46%)
Muscle spasms [A] †	7/75 (9.33%)	1/74 (1.35%)

	Chemotherapy + Pertuzumab	Chemotherapy
	Affected/At Risk (%)	Affected/At Risk (%)
Musculoskeletal pain [A] †	5/75 (6.67%)	2/74 (2.7%)
Myalgia [A] †	5/75 (6.67%)	6/74 (8.11%)
Pain in extremity [A] †	6/75 (8%)	5/74 (6.76%)
Nervous system disorders		
Dizziness [A] †	9/75 (12%)	6/74 (8.11%)
Dysgeusia [A] †	10/75 (13.33%)	5/74 (6.76%)
Headache [A] †	16/75 (21.33%)	8/74 (10.81%)
Lethargy [A] †	4/75 (5.33%)	2/74 (2.7%)
Neuropathy peripheral [A] †	11/75 (14.67%)	4/74 (5.41%)
Paraesthesia [A] †	4/75 (5.33%)	4/74 (5.41%)
Peripheral sensory neuropathy [A] †	8/75 (10.67%)	4/74 (5.41%)
Psychiatric disorders		
Insomnia [A] †	6/75 (8%)	5/74 (6.76%)
Reproductive system and breast disorders		
Vaginal discharge [A] †	4/75 (5.33%)	0/74 (0%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] †	5/75 (6.67%)	4/74 (5.41%)
Dyspnoea [A] †	8/75 (10.67%)	5/74 (6.76%)
Epistaxis [A] †	14/75 (18.67%)	3/74 (4.05%)
Skin and subcutaneous tissue disorders		
Alopecia [A] †	22/75 (29.33%)	25/74 (33.78%)
Dry skin [A] †	4/75 (5.33%)	1/74 (1.35%)
Erythema [A] †	5/75 (6.67%)	2/74 (2.7%)

	Chemotherapy + Pertuzumab	Chemotherapy
	Affected/At Risk (%)	Affected/At Risk (%)
Nail disorder [A] †	8/75 (10.67%)	0/74 (0%)
Pruritus [A] †	7/75 (9.33%)	9/74 (12.16%)
Rash [A] †	17/75 (22.67%)	7/74 (9.46%)
Vascular disorders		
Flushing [A] †	5/75 (6.67%)	2/74 (2.7%)
Hypertension [A] †	6/75 (8%)	0/74 (0%)
Phlebitis [A] †	3/75 (4%)	5/74 (6.76%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA 13.1
B Term from vocabulary, MedDRA13.1

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 after the first publication or presentation that involves the overall study. Sponsor may request that confidential information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

Results Point of Contact:

Name/Official Title: Medical Communications
Organization: Hoffmann- LaRoche
Phone: 800-821-8590
Email: genentech@druginfo.com