ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 11/04/2014

A Study of Tarceva (Erlotinib) in Combination With Avastin (Bevacizumab) in Patients With Advanced Non-Small Cell Lung Cancer.

This study has been completed.

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT00531960

Purpose

This 2 arm study will compare the efficacy and safety of Tarceva plus Avastin, and chemotherapy plus Avastin, in the first-line treatment of patients with advanced non-small cell lung cancer. Patients will be randomized to receive either Tarceva 150mg p.o. daily plus Avastin 15mg/kg i.v. every 3 weeks, or standard platinum-based chemotherapy (4-6 cycles) plus Avastin. The anticipated time on study treatment is until disease progression, and the target sample size is 100-500 individuals.

Condition	Intervention	Phase
Non-Small Cell Lung Cancer	Drug: Erlotinib Drug: Bevacizumab Drug: Standard platinum-based chemotherapy	Phase 2

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study
Official Title: A Randomized, Open-label Study Comparing the Anti-tumor Effect of Treatment With Tarceva Plus Avastin Versus Chemotherapy Plus Avastin in Patients With Advanced Non-small Cell Lung Cancer

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Percentage of Participants With Disease Progression or Death [Time Frame: Screening, end of every 2nd cycle through Cycle 8 (21-day cycles), and every 12 weeks thereafter until the end of study and final analysis up to a maximum of 42 months.] [Designated as safety issue: No]

  Progression-free survival (PFS) was defined as the time from randomization to disease progression or death, from any cause. Progressive disease (PD) was defined according to Response Criteria in Solid Tumors (RECIST) version (V) 1.0. For target lesions (TLs), progressive disease (PD) was defined as at least a 20 percent (%) increase in the sum of the longest diameter (SLD), taking as reference the smallest SLD recorded since the start of treatment. For non-target lesions (NTLs), PD was defined as unequivocal progression of existing NTLs. Participants were censored at the date of last post-baseline (BL) tumor assessment where non-progression was documented. If no post-BL tumor assessment was available, the participant was censored at date of randomization.
- PFS [Time Frame: Screening, end of every 2nd cycle through Cycle 8 (21-day cycles), and every 12 weeks thereafter until the end of study and final analysis up to a maximum of 42 months.] [Designated as safety issue: No]

  The median time, in weeks, from randomization to PFS event. Participants were censored at the date of last post-BL tumor assessment where non-progression was documented. If no post-BL tumor assessment was available, the participant was censored at date of randomization. PFS was estimated using Kaplan-Meier methodology.

Secondary Outcome Measures:

- Percentage of Participants Who Died [Time Frame: Screening, Days 1, 8, and 21 of Cycles 1-8 (21-day cycles), and every 12 weeks thereafter until the end of study and final analysis up to a maximum of 42 months.] [Designated as safety issue: No]

  Overall survival (OS) was defined as the time from randomization to the date of death, due to any cause. Participants were censored at final analysis at the date the participant was last known to be alive.
- OS [Time Frame: Screening, Days 1, 8, and 21 of Cycles 1-8 (21-day cycles), and every 12 weeks thereafter until the end of study and final analysis up to a maximum of 42 months.] [Designated as safety issue: No]

  The median time, in months, from randomization to OS event. Participants were censored at final analysis at the date the participant was last known to be alive.
- Percentage of Participants With a Best Overall Response (BOR) of Confirmed Complete Response (CR) or Partial Response (PR) According to RECIST V 1.0 [Time Frame: Screening, end of every 2nd cycle through Cycle 8 (21-day cycles), and every 12 weeks thereafter until the end of study and final analysis up to a maximum of 42 months.] [Designated as safety issue: No]

  BOR was defined as the best response recorded from randomization until disease progression/recurrence or death, taking as reference for PD the smallest measurement (nadir) recorded since treatment started. Assignment of PR of CR required confirmation of tumor measurement changes by repeat assessments performed no less than 4 weeks after criteria for response was first met. For TLs, CR was defined as the disappearance of all TLs; and PR was defined as at least a 30% decrease in the SLD of the TLs, taking BL SLD as reference. For NTLs, CR was defined as the disappearance of all NTLs and normalization of tumor marker levels. The 95% CI for one sample binomial was calculated using the Pearson-Clopper method.
- Percentage of Participants With Disease Control According to RECIST V 1.0 [Time Frame: Screening, end of every 2nd cycle through Cycle 8 (21-day cycles), and every 12 weeks thereafter until the end of study and final analysis, 12 months after the last participant's 1st visit] [Designated as safety issue: No]

  Disease control was defined as a BOR of CR, PR, or SD according to RECIST V 1.0 for at least 4 weeks at any time during randomized treatment or disease stabilization, after study entry. Participants without a post-BL assessment of response were considered as having no disease control. The 95% CI for the one sample binomial was calculated using the Pearson-Clopper method.

Enrollment: 124
Study Start Date: January 2008
Primary Completion Date: January 2010
Study Completion Date: January 2010

Arms	Assigned Interventions
Active Comparator: Bevacizumab, Chemotherapy Participants received bevacizumab, 15 milligrams (mg) per (/) kilogram (kg), intravenously (IV), on Day 1 of Cycles 1 through 7 until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received 4 to 6 cycles of a standard platinum-containing regimen of chemotherapy: either gemcitabine, 1250 mg/ square meter (m^2), IV, on Days 1 and 8 of Cycles 1 through 4 or 6, and cisplatin 80 mg/m^2, IV, on Day 1 of Cycles 1 through 4 or 6; or paclitaxel, 200 mg/m^2, IV, and carboplatin area under the curve (AUC) 6 mg/ milliliter (ml) multiplied by (*) minute (min) on Day 1 of Cycles 1 through 4 or 6. The chemotherapy regimen and number of cycles was up to the discretion of the investigator.	Drug: Bevacizumab 15 mg/kg, IV, Day 1 of Cycles 1 through 7 Other Names: Avastin Drug: Standard platinum-based chemotherapy At the discretion of the investigator
Experimental: Bevacizumab, Erlotinib Participants received bevacizumab, 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received erlotinib, 150 mg, orally (PO), daily until disease progression, unacceptable toxicity, death, or withdrawal.	Drug: Erlotinib 150 mg, PO, daily Other Names: Tarceva Drug: Bevacizumab 15 mg/kg, IV, Day 1 of Cycles 1 through 7 Other Names: Avastin

Eligibility

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

Criteria

Inclusion Criteria:

- adult patients, >=18 years of age;

- advanced (stage IIIb and IV) non-small cell lung cancer;
- measurable disease;
- ECOG PS 0-1.

Exclusion Criteria:

- prior chemotherapy or treatment with another systemic anti-cancer agent;
- radiotherapy within 4 weeks prior to first dose of study treatment;
- CNS metastases;
- other malignancies in past 5 years, except for adequately treated cancer in situ of the cervix, basal or squamous cell skin cancer.

Contacts and Locations

Locations

Australia, Victoria
East Bentleigh, Victoria, Australia, VIC 3165
Geelong, Victoria, Australia, 3220

Belgium
Leuven, Belgium, 3000

France
Bayonne, France, 64100
Dijon, France, 21079
Le Mans, France, 72037
Marseille, France, 13273
Paris, France, 75674
Strasbourg, France, 67091
Vandoeuvre-les-nancy, France, 54511

Italy
Aviano, Friuli-Venezia Giulia, Italy, 33081
Milano, Lombardia, Italy, 20133
Ancona, Marche, Italy, 60121
Lido Di Camaiore, Toscana, Italy, 55043

Korea, Republic of
Bundang City, Korea, Republic of, 463-802
Daegu, Korea, Republic of, 700-712
Gyeonggi-do, Korea, Republic of, 411-769
Incheon, Korea, Republic of, 405-760
Seoul, Korea, Republic of, 120-752
Seoul, Korea, Republic of, 110-744
Seoul, Korea, Republic of, 135-710
Seoul, Korea, Republic of, 138-736
Seoul, Korea, Republic of, 137-807
Suwon, Korea, Republic of

Lithuania
Kaunas, Lithuania, 50009

Vilnius, Lithuania, 08660

Netherlands

's Hertogenbosch, Netherlands, 5211 RW
Amsterdam, Netherlands, 1007 MB
Eindhoven, Netherlands, 5623 EJ
Groningen, Netherlands, 9713 GZ
Heerlen, Netherlands, 6419 PC
Maastricht, Netherlands, 6229 HX
Rotterdam, Netherlands, 3045 PM

Poland

Lodz, Poland, 91-520
Lublin, Poland, 20-950
Otwock, Poland, 05-400

Romania

Bucuresti, Romania, 022328
Cluj Napoca, Romania, 400015
Timisoara, Romania, 1900

Singapore

Singapore, Singapore, 119074

Spain

Alicante, Alicante, Spain, 3010
Barcelona, Barcelona, Spain, 08035
La Coruña, La Coruña, Spain, 15006
Madrid, Madrid, Spain, 28041
Madrid, Madrid, Spain, 28046
Madrid, Madrid, Spain, 28222
Malaga, Malaga, Spain, 29010
Sevilla, Sevilla, Spain, 41014

Taiwan

Changhua, Taiwan, 500
Kaohsiung, Taiwan, 00833
Tainan, Taiwan, 710
Taipei, Taiwan
Taipei, Taiwan, 112
Taipei, Taiwan, 114

United Kingdom

Dudley, United Kingdom, DY1 2HQ
Guildford, United Kingdom, GU2 7XX
Manchester, United Kingdom, M2O 4BX

Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Study Results

Participant Flow

Reporting Groups

	Description
Bevacizumab Plus (+) Chemotherapy	Participants received bevacizumab 15 milligrams per kilogram (mg/kg), intravenously (IV), on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received a maximum of up to 6 cycles (12-18 weeks) with EITHER a gemicitabine/cisplatin regimen (gemcitabine 1250 milligrams per square meter [mg/m^2], IV, on Days 1 and 8 of up to 6 cycles of 21 days, and cisplatin 80 mg/m^2, IV, on Day 1 of up to 6 cycles of 21 days); OR a carboplatin/paclitaxel regimen (paclitaxel 200 mg/m^2, IV, followed by carboplatin 6 milligrams per milliliter multiplied by minute [mg/mL*min] on Day 1 of up to 6 cycles of 21 days). The chemotherapy regimen and number of cycles was up to the discretion of the investigator.
Bevacizumab + Erlotinib	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received erlotinib 150 mg tablets, orally (PO), daily until disease progression, unacceptable toxicity, death, or withdrawal.

Overall Study

	Bevacizumab Plus (+) Chemotherapy	Bevacizumab + Erlotinib
Started	61	63
Completed	0	0
Not Completed	61	63
Adverse Event	5	4
Death	3	2
Lack of Efficacy	42	41
Violation of Selection Criteria	2	0
Refused Treatment	5	6
Not Specified	4	10

Baseline Characteristics

Analysis Population Description

Full analysis set (FAS): all randomized participants.

Reporting Groups

	Description
Bevacizumab + Chemotherapy	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received a maximum of up to 6 cycles (12-18 weeks) with EITHER a gemicitabine/cisplatin regimen (gemcitabine 1250 mg/m^2, IV, on Days 1 and 8 of up to 6 cycles of 21 days, and cisplatin 80 mg/m^2, IV, on Day 1 of up to 6 cycles of 21 days); OR a carboplatin/paclitaxel regimen (paclitaxel 200 mg/m^2, IV, followed by carboplatin 6 mg/mL*min on Day 1 of up to 6 cycles of 21 days). The chemotherapy regimen and number of cycles was up to the discretion of the investigator.
Bevacizumab + Erlotinib	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received erlotinib 150 mg tablets, PO, daily until disease progression, unacceptable toxicity, death, or withdrawal.

Baseline Measures

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib	Total
Number of Participants	61	63	124
Age, Continuous [units: years] Mean (Standard Deviation)	58.0 (9.55)	61.0 (10.94)	59.53 (10.34)
Gender, Male/Female [units: participants]			
Female	25	26	51
Male	36	37	73

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Disease Progression or Death

Measure Description	Progression-free survival (PFS) was defined as the time from randomization to disease progression or death, from any cause. Progressive disease (PD) was defined according to Response Criteria in Solid Tumors (RECIST) version (V) 1.0. For target lesions (TLs), progressive disease (PD) was defined as at least a 20 percent (%) increase in the sum of the longest diameter (SLD), taking as reference the smallest SLD recorded since the start of treatment. For non-target lesions (NTLs), PD was defined as unequivocal progression of existing NTLs. Participants were censored at the date of last post-baseline (BL) tumor assessment where non-progression was documented. If no post-BL tumor assessment was available, the participant was censored at date of randomization.
Time Frame	Screening, end of every 2nd cycle through Cycle 8 (21-day cycles), and every 12 weeks thereafter until the end of study and final analysis up to a maximum of 42 months.
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Bevacizumab + Chemotherapy	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received a maximum of up to 6 cycles (12-18 weeks) with EITHER a gemicitabine/cisplatin regimen (gemcitabine 1250 mg/m^2, IV, on Days 1 and 8 of up to 6 cycles of 21 days, and cisplatin 80 mg/m^2, IV, on Day 1 of up to 6 cycles of 21 days); OR a carboplatin/paclitaxel regimen (paclitaxel 200 mg/m^2, IV, followed by carboplatin 6 mg/mL*min on Day 1 of up to 6 cycles of 21 days). The chemotherapy regimen and number of cycles was up to the discretion of the investigator.
Bevacizumab + Erlotinib	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received erlotinib 150 mg tablets, PO, daily until disease progression, unacceptable toxicity, death, or withdrawal.

Measured Values

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
Number of Participants Analyzed	61	63
Percentage of Participants With Disease Progression or Death [units: percentage of participants]	72.1	76.2

2. Primary Outcome Measure:

Measure Title	PFS

Measure Description	The median time, in weeks, from randomization to PFS event. Participants were censored at the date of last post-BL tumor assessment where non-progression was documented. If no post-BL tumor assessment was available, the participant was censored at date of randomization. PFS was estimated using Kaplan-Meier methodology.
Time Frame	Screening, end of every 2nd cycle through Cycle 8 (21-day cycles), and every 12 weeks thereafter until the end of study and final analysis up to a maximum of 42 months.
Safety Issue?	No

Analysis Population Description

FAS; only participants with an event (disease progression or death) were included in the analysis.

Reporting Groups

	Description
Bevacizumab + Chemotherapy	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received a maximum of up to 6 cycles (12-18 weeks) with EITHER a gemicitabine/cisplatin regimen (gemcitabine 1250 mg/m^2, IV, on Days 1 and 8 of up to 6 cycles of 21 days, and cisplatin 80 mg/m^2, IV, on Day 1 of up to 6 cycles of 21 days); OR a carboplatin/paclitaxel regimen (paclitaxel 200 mg/m^2, IV, followed by carboplatin 6 mg/mL*min on Day 1 of up to 6 cycles of 21 days). The chemotherapy regimen and number of cycles was up to the discretion of the investigator.
Bevacizumab + Erlotinib	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received erlotinib 150 mg tablets, PO, daily until disease progression, unacceptable toxicity, death, or withdrawal.

Measured Values

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
Number of Participants Analyzed	44	48
PFS [units: weeks] Median (95% Confidence Interval)	34.6 (25.0 to 42.4)	23.4 (17.4 to 45.1)

Statistical Analysis 1 for PFS

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

Statistical Test of Hypothesis	P-Value	0.8060
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.05
	Confidence Interval	(2-Sided) 95% 0.70 to 1.59
	Estimation Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Died
Measure Description	Overall survival (OS) was defined as the time from randomization to the date of death, due to any cause. Participants were censored at final analysis at the date the participant was last known to be alive.
Time Frame	Screening, Days 1, 8, and 21 of Cycles 1-8 (21-day cycles), and every 12 weeks thereafter until the end of study and final analysis up to a maximum of 42 months.
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Bevacizumab + Chemotherapy	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received a maximum of up to 6 cycles (12-18 weeks) with EITHER a gemicitabine/cisplatin regimen (gemcitabine 1250 mg/m^2, IV, on Days 1 and 8 of up to 6 cycles of 21 days, and cisplatin 80 mg/m^2, IV, on Day 1 of up to 6 cycles of 21 days); OR a carboplatin/paclitaxel regimen (paclitaxel 200 mg/m^2, IV, followed by carboplatin 6 mg/mL*min on Day 1 of up to 6 cycles of 21 days). The chemotherapy regimen and number of cycles was up to the discretion of the investigator.
Bevacizumab + Erlotinib	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received erlotinib 150 mg tablets, PO, daily until disease progression, unacceptable toxicity, death, or withdrawal.

Measured Values

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
Number of Participants Analyzed	61	63
Percentage of Participants Who Died [units: percentage of participants]	45.9	52.4

4. Secondary Outcome Measure:

Measure Title	OS
Measure Description	The median time, in months, from randomization to OS event. Participants were censored at final analysis at the date the participant was last known to be alive.
Time Frame	Screening, Days 1, 8, and 21 of Cycles 1-8 (21-day cycles), and every 12 weeks thereafter until the end of study and final analysis up to a maximum of 42 months.
Safety Issue?	No

Analysis Population Description

FAS; only participants who died were included in this analysis.

Reporting Groups

	Description
Bevacizumab + Chemotherapy	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received a maximum of up to 6 cycles (12-18 weeks) with EITHER a gemicitabine/cisplatin regimen (gemcitabine 1250 mg/m^2, IV, on Days 1 and 8 of up to 6 cycles of 21 days, and cisplatin 80 mg/m^2, IV, on Day 1 of up to 6 cycles of 21 days); OR a carboplatin/paclitaxel regimen (paclitaxel 200 mg/m^2, IV, followed by carboplatin 6 mg/mL*min on Day 1 of up to 6 cycles of 21 days). The chemotherapy regimen and number of cycles was up to the discretion of the investigator.
Bevacizumab + Erlotinib	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received erlotinib 150 mg tablets, PO, daily until disease progression, unacceptable toxicity, death, or withdrawal.

Measured Values

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
Number of Participants Analyzed	28	33
OS [units: months]	NA (12.7 to NA) [1]	16.4 (11.0 to NA) [2]

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
Median (95% Confidence Interval)		

[1] The median and upper limit of the 95% confidence interval (CI) could not be calculated due to the large number of censored events.
[2] The upper limit of the 95% CI could not be calculated due to the large number of censored events.

Statistical Analysis 1 for OS

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

Statistical Test of Hypothesis	P-Value	0.4063
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	1.24
	Confidence Interval	(2-Sided) 95% 0.75 to 2.05
	Estimation Comments	[Not specified]

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Best Overall Response (BOR) of Confirmed Complete Response (CR) or Partial Response (PR) According to RECIST V 1.0
Measure Description	BOR was defined as the best response recorded from randomization until disease progression/recurrence or death, taking as reference for PD the smallest measurement (nadir) recorded since treatment started. Assignment of PR of CR required confirmation of tumor measurement changes by repeat assessments performed no less than 4 weeks after criteria for response was first met. For TLs, CR was defined as the disappearance of all TLs; and PR was defined as at least a 30% decrease in the SLD of the TLs, taking BL SLD as reference. For NTLs, CR was defined as the disappearance of all NTLs and normalization of tumor marker levels. The 95% CI for one sample binomial was calculated using the Pearson-Clopper method.

Time Frame	Screening, end of every 2nd cycle through Cycle 8 (21-day cycles), and every 12 weeks thereafter until the end of study and final analysis up to a maximum of 42 months.
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Bevacizumab + Chemotherapy	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received a maximum of up to 6 cycles (12-18 weeks) with EITHER a gemicitabine/cisplatin regimen (gemcitabine 1250 mg/m^2, IV, on Days 1 and 8 of up to 6 cycles of 21 days, and cisplatin 80 mg/m^2, IV, on Day 1 of up to 6 cycles of 21 days); OR a carboplatin/paclitaxel regimen (paclitaxel 200 mg/m^2, IV, followed by carboplatin 6 mg/mL*min on Day 1 of up to 6 cycles of 21 days). The chemotherapy regimen and number of cycles was up to the discretion of the investigator.
Bevacizumab + Erlotinib	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received erlotinib 150 mg tablets, PO, daily until disease progression, unacceptable toxicity, death, or withdrawal.

Measured Values

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
Number of Participants Analyzed	61	63
Percentage of Participants With a Best Overall Response (BOR) of Confirmed Complete Response (CR) or Partial Response (PR) According to RECIST V 1.0 [units: percentage of participants] Number (95% Confidence Interval)	44.3 (31.5 to 57.6)	27.0 (16.6 to 39.7)

Statistical Analysis 1 for Percentage of Participants With a Best Overall Response (BOR) of Confirmed Complete Response (CR) or Partial Response (PR) According to RECIST V 1.0

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

Statistical Test of Hypothesis	P-Value	0.0444
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Difference in Response Rates]
	Estimated Value	-17.28
	Confidence Interval	(2-Sided) 95% -34.8 to 0.3
	Estimation Comments	The 95% CI for the difference of 2 rates was determined by using the Hauck-Anderson method.

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Disease Control According to RECIST V 1.0
Measure Description	Disease control was defined as a BOR of CR, PR, or SD according to RECIST V 1.0 for at least 4 weeks at any time during randomized treatment or disease stabilization, after study entry. Participants without a post-BL assessment of response were considered as having no disease control. The 95% CI for the one sample binomial was calculated using the Pearson-Clopper method.
Time Frame	Screening, end of every 2nd cycle through Cycle 8 (21-day cycles), and every 12 weeks thereafter until the end of study and final analysis, 12 months after the last participant's 1st visit
Safety Issue?	No

Analysis Population Description
FAS

Reporting Groups

	Description
Bevacizumab + Chemotherapy	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received a maximum of up to 6 cycles (12-18 weeks) with EITHER a gemicitabine/cisplatin regimen (gemcitabine 1250 mg/m^2, IV, on Days 1 and 8 of up to 6 cycles of 21 days, and cisplatin 80 mg/m^2, IV, on Day 1 of up to 6 cycles of 21 days); OR a carboplatin/paclitaxel regimen (paclitaxel 200 mg/m^2, IV, followed by carboplatin 6 mg/mL*min on Day 1 of up to 6 cycles of 21 days). The chemotherapy regimen and number of cycles was up to the discretion of the investigator.

	Description
Bevacizumab + Erlotinib	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received erlotinib 150 mg tablets, PO, daily until disease progression, unacceptable toxicity, death, or withdrawal.

Measured Values

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
Number of Participants Analyzed	61	63
Percentage of Participants With Disease Control According to RECIST V 1.0 [units: percentage of participants] Number (95% Confidence Interval)	85.2 (73.8 to 93.0)	73.0 (60.3 to 83.4)

Statistical Analysis 1 for Percentage of Participants With Disease Control According to RECIST V 1.0

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

Statistical Test of Hypothesis	P-Value	0.0944
	Comments	[Not specified]
	Method	Chi-squared
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Other [Difference in Disease Control Rates]
	Estimated Value	-12.2
	Confidence Interval	(2-Sided) 95% -27.3 to 2.8
	Estimation Comments	The 95% CI for the difference in disease control was determined using the Hauck-Anderson method.

Reported Adverse Events

Time Frame	Adverse events (AEs) and serious AEs (SAEs) were reported from Screening through Day 84. Unrelated events were reported up to 28 days after last study drug treatment, related events were reported until resolution or stabilization
Additional Description	All participants who received at least 1 dose of the study treatment and had at least 1 safety follow-up, whether withdrawn prematurely or not, were included in the safety analysis population.

Reporting Groups

	Description
Bevacizumab + Chemotherapy	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received a maximum of up to 6 cycles (12-18 weeks) with EITHER a gemicitabine/cisplatin regimen (gemcitabine 1250 mg/m^2, IV, on Days 1 and 8 of up to 6 cycles of 21 days, and cisplatin 80 mg/m^2, IV, on Day 1 of up to 6 cycles of 21 days); OR a carboplatin/paclitaxel regimen (paclitaxel 200 mg/m^2, IV, followed by carboplatin 6 mg/mL*min on Day 1 of up to 6 cycles of 21 days). The chemotherapy regimen and number of cycles was up to the discretion of the investigator.
Bevacizumab + Erlotinib	Participants received bevacizumab 15 mg/kg, IV, on Day 1 of Cycles 1 through 7 (21 day cycles) until disease progression, unacceptable toxicity, death, or withdrawal. Participants also received erlotinib 150 mg tablets, PO, daily until disease progression, unacceptable toxicity, death, or withdrawal.

Serious Adverse Events

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Total	22/60 (36.67%)	17/63 (26.98%)
Blood and lymphatic system disorders		
Anaemia [A] *	2/60 (3.33%)	0/63 (0%)
Febrile neutropenia [A] *	2/60 (3.33%)	0/63 (0%)
Neutropenia [A] *	2/60 (3.33%)	0/63 (0%)
Pancytopenia [A] *	1/60 (1.67%)	0/63 (0%)
Thrombocytopenia [A] *	2/60 (3.33%)	0/63 (0%)
Cardiac disorders		
Myocardial infarction [A] *	0/60 (0%)	1/63 (1.59%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Gastrointestinal disorders		
Enterovesical fistula [A] *	0/60 (0%)	1/63 (1.59%)
Gastric ulcer [A] *	0/60 (0%)	1/63 (1.59%)
Vomiting [A] *	1/60 (1.67%)	0/63 (0%)
General disorders		
Death [A] *	1/60 (1.67%)	0/63 (0%)
Infections and infestations		
Biliary tract infection [A] *	0/60 (0%)	1/63 (1.59%)
Bronchitis [A] *	1/60 (1.67%)	1/63 (1.59%)
Catheter site infection [A] *	1/60 (1.67%)	0/63 (0%)
Dermatitis infected [A] *	0/60 (0%)	1/63 (1.59%)
Folliculitis [A] *	0/60 (0%)	1/63 (1.59%)
Gastroenteritis [A] *	1/60 (1.67%)	0/63 (0%)
Pneumonia [A] *	3/60 (5%)	0/63 (0%)
Septic shock [A] *	1/60 (1.67%)	0/63 (0%)
Urinary tract infection [A] *	1/60 (1.67%)	0/63 (0%)
Viral infection [A] *	0/60 (0%)	1/63 (1.59%)
Investigations		
Weight decreased [A] *	0/60 (0%)	1/63 (1.59%)
Metabolism and nutrition disorders		
Decreased appetite [A] *	0/60 (0%)	1/63 (1.59%)
Gout [A] *	0/60 (0%)	1/63 (1.59%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Prostate cancer [A] *	1/60 (1.67%)	0/63 (0%)
Tumour associated fever [A] *	0/60 (0%)	1/63 (1.59%)
Nervous system disorders		
Cerebral haemorrhage [A] *	1/60 (1.67%)	0/63 (0%)
Ischaemic stroke [A] *	0/60 (0%)	1/63 (1.59%)
Posterior reversible encephalopathy syndrome [A] *	1/60 (1.67%)	0/63 (0%)
Spinal cord compression [A] *	1/60 (1.67%)	0/63 (0%)
Psychiatric disorders		
Confusional state [A] *	1/60 (1.67%)	0/63 (0%)
Renal and urinary disorders		
Haematuria [A] *	0/60 (0%)	1/63 (1.59%)
Respiratory, thoracic and mediastinal disorders		
Acute pulmonary oedema [A] *	1/60 (1.67%)	0/63 (0%)
Dyspnoea [A] *	1/60 (1.67%)	0/63 (0%)
Haemoptysis [A] *	2/60 (3.33%)	0/63 (0%)
Pleural effusion [A] *	0/60 (0%)	1/63 (1.59%)
Pulmonary Oedema [A] *	1/60 (1.67%)	0/63 (0%)
Pulmonary embolism [A] *	3/60 (5%)	2/63 (3.17%)
Pulmonary haemorrhage [A] *	0/60 (0%)	1/63 (1.59%)
Skin and subcutaneous tissue disorders		
Rash [A] *	0/60 (0%)	1/63 (1.59%)
Vascular disorders		

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Deep vein thrombosis [A] *	1/60 (1.67%)	1/63 (1.59%)
Haematoma [A] *	1/60 (1.67%)	1/63 (1.59%)
Jugular vein thrombosis [A] *	0/60 (0%)	1/63 (1.59%)
Peripheral embolism [A] *	1/60 (1.67%)	0/63 (0%)
Venous thrombosis limb [A] *	0/60 (0%)	1/63 (1.59%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.1)

Other Adverse Events
Frequency Threshold Above Which Other Adverse Events are Reported: 0%

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Total	58/60 (96.67%)	60/63 (95.24%)
Blood and lymphatic system disorders		
Anaemia [A] *	18/60 (30%)	2/63 (3.17%)
Febrile neutropenia [A] *	2/60 (3.33%)	0/63 (0%)
Leukocytosis [A] *	1/60 (1.67%)	1/63 (1.59%)
Leukopenia [A] *	17/60 (28.33%)	0/63 (0%)
Lymphocytosis [A] *	1/60 (1.67%)	0/63 (0%)
Neutropenia [A] *	24/60 (40%)	0/63 (0%)
Thrombocytopenia [A] *	16/60 (26.67%)	1/63 (1.59%)
Cardiac disorders		
Acute coronary syndrome [A] *	0/60 (0%)	1/63 (1.59%)
Atrial fibrillation [A] *	1/60 (1.67%)	0/63 (0%)
Atrioventricular block [A] *	1/60 (1.67%)	0/63 (0%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Cardiac failure congestive [A] *	0/60 (0%)	1/63 (1.59%)
Cardiovascular disorder [A] *	1/60 (1.67%)	1/63 (1.59%)
Palpitations [A] *	1/60 (1.67%)	2/63 (3.17%)
Ear and labyrinth disorders		
Cerumen impaction [A] *	1/60 (1.67%)	0/63 (0%)
Tinnitus [A] *	4/60 (6.67%)	1/63 (1.59%)
Vertigo [A] *	1/60 (1.67%)	0/63 (0%)
Eye disorders		
Blepharitis [A] *	0/60 (0%)	2/63 (3.17%)
Cataract [A] *	0/60 (0%)	1/63 (1.59%)
Conjunctivitis [A] *	0/60 (0%)	2/63 (3.17%)
Diplopia [A] *	1/60 (1.67%)	1/63 (1.59%)
Dry eye [A] *	0/60 (0%)	1/63 (1.59%)
Eye pain [A] *	0/60 (0%)	2/63 (3.17%)
Glaucoma [A] *	1/60 (1.67%)	0/63 (0%)
Vision blurred [A] *	3/60 (5%)	2/63 (3.17%)
Gastrointestinal disorders		
Abdominal discomfort [A] *	2/60 (3.33%)	1/63 (1.59%)
Abdominal distension [A] *	1/60 (1.67%)	3/63 (4.76%)
Abdominal pain [A] *	4/60 (6.67%)	7/63 (11.11%)
Abdominal pain upper [A] *	6/60 (10%)	4/63 (6.35%)
Anal fissure [A] *	0/60 (0%)	1/63 (1.59%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Anal fistula [A] *	1/60 (1.67%)	0/63 (0%)
Anal haemorrhage [A] *	0/60 (0%)	1/63 (1.59%)
Constipation [A] *	12/60 (20%)	7/63 (11.11%)
Dental caries [A] *	0/60 (0%)	1/63 (1.59%)
Diarrhoea [A] *	15/60 (25%)	27/63 (42.86%)
Dry mouth [A] *	1/60 (1.67%)	0/63 (0%)
Duodenitis [A] *	0/60 (0%)	1/63 (1.59%)
Dyspepsia [A] *	6/60 (10%)	7/63 (11.11%)
Dysphagia [A] *	1/60 (1.67%)	1/63 (1.59%)
Eructation [A] *	1/60 (1.67%)	0/63 (0%)
Flatulence [A] *	1/60 (1.67%)	0/63 (0%)
Frequent bowel movements [A] *	0/60 (0%)	1/63 (1.59%)
Gastric ulcer [A] *	1/60 (1.67%)	0/63 (0%)
Gastritis [A] *	1/60 (1.67%)	1/63 (1.59%)
Gastrooesophageal reflux disease [A] *	0/60 (0%)	1/63 (1.59%)
Gingival bleeding [A] *	5/60 (8.33%)	3/63 (4.76%)
Gingival pain [A] *	1/60 (1.67%)	0/63 (0%)
Gingival swelling [A] *	0/60 (0%)	1/63 (1.59%)
Gingivitis [A] *	0/60 (0%)	1/63 (1.59%)
Haematochezia [A] *	0/60 (0%)	2/63 (3.17%)
Haemorrhoidal haemorrhage [A] *	2/60 (3.33%)	1/63 (1.59%)
Haemorrhoids [A] *	0/60 (0%)	5/63 (7.94%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Mouth ulceration [A] *	1/60 (1.67%)	1/63 (1.59%)
Nausea [A] *	37/60 (61.67%)	12/63 (19.05%)
Odynophagia [A] *	0/60 (0%)	1/63 (1.59%)
Oral pruritus [A] *	0/60 (0%)	1/63 (1.59%)
Periodontitis [A] *	2/60 (3.33%)	1/63 (1.59%)
Proctalgia [A] *	0/60 (0%)	3/63 (4.76%)
Rectal haemorrhage [A] *	2/60 (3.33%)	0/63 (0%)
Stomatitis [A] *	8/60 (13.33%)	9/63 (14.29%)
Toothache [A] *	5/60 (8.33%)	1/63 (1.59%)
Vomiting [A] *	23/60 (38.33%)	5/63 (7.94%)
General disorders		
Asthenia [A] *	13/60 (21.67%)	7/63 (11.11%)
Axillary pain [A] *	0/60 (0%)	1/63 (1.59%)
Chest discomfort [A] *	4/60 (6.67%)	5/63 (7.94%)
Chest pain [A] *	6/60 (10%)	6/63 (9.52%)
Chills [A] *	2/60 (3.33%)	0/63 (0%)
Discomfort [A] *	1/60 (1.67%)	0/63 (0%)
Fatigue [A] *	19/60 (31.67%)	14/63 (22.22%)
Feeling cold [A] *	0/60 (0%)	1/63 (1.59%)
Hunger [A] *	0/60 (0%)	1/63 (1.59%)
Influenza like illness [A] *	0/60 (0%)	2/63 (3.17%)
Malaise [A] *	1/60 (1.67%)	0/63 (0%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Mucosal inflammation [A] *	4/60 (6.67%)	5/63 (7.94%)
Oedema [A] *	2/60 (3.33%)	1/63 (1.59%)
Oedema peripheral [A] *	2/60 (3.33%)	1/63 (1.59%)
Pain [A] *	0/60 (0%)	4/63 (6.35%)
Pyrexia [A] *	3/60 (5%)	6/63 (9.52%)
Xerosis [A] *	0/60 (0%)	1/63 (1.59%)
Hepatobiliary disorders		
Hepatic function abnormal [A] *	0/60 (0%)	1/63 (1.59%)
Hyperbilirubinaemia [A] *	0/60 (0%)	1/63 (1.59%)
Immune system disorders		
Hypersensitivity [A] *	1/60 (1.67%)	0/63 (0%)
Infections and infestations		
Bronchitis [A] *	0/60 (0%)	3/63 (4.76%)
Candidiasis [A] *	0/60 (0%)	1/63 (1.59%)
Catheter site infection [A] *	1/60 (1.67%)	0/63 (0%)
Cystitis [A] *	1/60 (1.67%)	0/63 (0%)
Eye infection [A] *	0/60 (0%)	1/63 (1.59%)
Folliculitis [A] *	0/60 (0%)	3/63 (4.76%)
Fungal skin infection [A] *	1/60 (1.67%)	0/63 (0%)
Hepatitis B [A] *	0/60 (0%)	1/63 (1.59%)
Influenza [A] *	0/60 (0%)	1/63 (1.59%)
Localised infection [A] *	0/60 (0%)	1/63 (1.59%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Lung infection [A] *	1/60 (1.67%)	0/63 (0%)
Nail infection [A] *	0/60 (0%)	1/63 (1.59%)
Nasopharyngitis [A] *	4/60 (6.67%)	4/63 (6.35%)
Onychomycosis [A] *	1/60 (1.67%)	0/63 (0%)
Oral herpes [A] *	1/60 (1.67%)	1/63 (1.59%)
Otitis externa [A] *	0/60 (0%)	1/63 (1.59%)
Paronychia [A] *	1/60 (1.67%)	8/63 (12.7%)
Rash pustular [A] *	0/60 (0%)	1/63 (1.59%)
Rhinitis [A] *	1/60 (1.67%)	1/63 (1.59%)
Skin infection [A] *	1/60 (1.67%)	1/63 (1.59%)
Tinea pedis [A] *	1/60 (1.67%)	0/63 (0%)
Tooth abscess [A] *	1/60 (1.67%)	0/63 (0%)
Tooth infection [A] *	1/60 (1.67%)	0/63 (0%)
Tuberculosis [A] *	0/60 (0%)	1/63 (1.59%)
Upper respiratory tract infection [A] *	5/60 (8.33%)	8/63 (12.7%)
Urinary tract infection [A] *	5/60 (8.33%)	6/63 (9.52%)
Injury, poisoning and procedural complications		
Incision site pain [A] *	0/60 (0%)	1/63 (1.59%)
Radiation skin injury [A] *	1/60 (1.67%)	0/63 (0%)
Wound complication [A] *	1/60 (1.67%)	0/63 (0%)
Investigations		
Alanine aminotransferase increased [A] *	1/60 (1.67%)	4/63 (6.35%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Aspartate aminotransferase increased [A] *	2/60 (3.33%)	3/63 (4.76%)
Blood alkaline phosphatase increased [A] *	0/60 (0%)	1/63 (1.59%)
Blood calcium decreased [A] *	0/60 (0%)	1/63 (1.59%)
Blood creatinine increased [A] *	3/60 (5%)	0/63 (0%)
Blood lactate dehydrogenase increased [A] *	2/60 (3.33%)	0/63 (0%)
Blood potassium decreased [A] *	1/60 (1.67%)	1/63 (1.59%)
Blood urea increased [A] *	2/60 (3.33%)	0/63 (0%)
Blood uric acid increased [A] *	1/60 (1.67%)	0/63 (0%)
Creatinine renal clearance decreased [A] *	0/60 (0%)	1/63 (1.59%)
Electrocardiogram T wave inversion [A] *	1/60 (1.67%)	0/63 (0%)
Glomerular filtration rate decreased [A] *	0/60 (0%)	1/63 (1.59%)
Lymphocyte count increased [A] *	1/60 (1.67%)	0/63 (0%)
Monocyte count increased [A] *	1/60 (1.67%)	0/63 (0%)
Platelet count decreased [A] *	1/60 (1.67%)	0/63 (0%)
Weight decreased [A] *	4/60 (6.67%)	3/63 (4.76%)
Weight increased [A] *	2/60 (3.33%)	0/63 (0%)
White blood cell count decreased [A] *	1/60 (1.67%)	0/63 (0%)
Metabolism and nutrition disorders		
Decreased appetite [A] *	23/60 (38.33%)	11/63 (17.46%)
Hypercholesterolaemia [A] *	0/60 (0%)	1/63 (1.59%)
Hyperglycaemia [A] *	2/60 (3.33%)	0/63 (0%)
Hyperkalaemia [A] *	5/60 (8.33%)	2/63 (3.17%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Hypertriglyceridaemia [A] *	1/60 (1.67%)	0/63 (0%)
Hyperuricaemia [A] *	2/60 (3.33%)	0/63 (0%)
Hypoalbuminaemia [A] *	0/60 (0%)	1/63 (1.59%)
Hypocalcaemia [A] *	1/60 (1.67%)	1/63 (1.59%)
Hypokalaemia [A] *	2/60 (3.33%)	1/63 (1.59%)
Hyponatraemia [A] *	1/60 (1.67%)	0/63 (0%)
Hypophagia [A] *	0/60 (0%)	1/63 (1.59%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	5/60 (8.33%)	3/63 (4.76%)
Arthritis [A] *	0/60 (0%)	1/63 (1.59%)
Back pain [A] *	6/60 (10%)	2/63 (3.17%)
Bone pain [A] *	1/60 (1.67%)	1/63 (1.59%)
Flank pain [A] *	1/60 (1.67%)	0/63 (0%)
Groin pain [A] *	0/60 (0%)	1/63 (1.59%)
Joint swelling [A] *	1/60 (1.67%)	0/63 (0%)
Muscle spasms [A] *	1/60 (1.67%)	3/63 (4.76%)
Muscular weakness [A] *	1/60 (1.67%)	2/63 (3.17%)
Musculoskeletal chest pain [A] *	0/60 (0%)	2/63 (3.17%)
Musculoskeletal pain [A] *	5/60 (8.33%)	1/63 (1.59%)
Myalgia [A] *	9/60 (15%)	5/63 (7.94%)
Neck pain [A] *	1/60 (1.67%)	2/63 (3.17%)
Osteitis [A] *	0/60 (0%)	1/63 (1.59%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Osteoarthritis [A] *	0/60 (0%)	2/63 (3.17%)
Pain in extremity [A] *	2/60 (3.33%)	3/63 (4.76%)
Pain in jaw [A] *	0/60 (0%)	1/63 (1.59%)
Rheumatoid arthritis [A] *	0/60 (0%)	1/63 (1.59%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Cancer pain [A] *	1/60 (1.67%)	0/63 (0%)
Nervous system disorders		
Ageusia [A] *	0/60 (0%)	1/63 (1.59%)
Cerebral infarction [A] *	0/60 (0%)	1/63 (1.59%)
Dizziness [A] *	4/60 (6.67%)	4/63 (6.35%)
Dysgeusia [A] *	1/60 (1.67%)	2/63 (3.17%)
Headache [A] *	7/60 (11.67%)	12/63 (19.05%)
Hyperaesthesia [A] *	1/60 (1.67%)	0/63 (0%)
Hypoaesthesia [A] *	2/60 (3.33%)	0/63 (0%)
Lethargy [A] *	1/60 (1.67%)	0/63 (0%)
Migraine [A] *	1/60 (1.67%)	0/63 (0%)
Neuropathy peripheral [A] *	10/60 (16.67%)	1/63 (1.59%)
Paraesthesia [A] *	5/60 (8.33%)	1/63 (1.59%)
Peripheral sensory neuropathy [A] *	5/60 (8.33%)	1/63 (1.59%)
Presyncope [A] *	1/60 (1.67%)	0/63 (0%)
Restless legs syndrome [A] *	0/60 (0%)	1/63 (1.59%)
Sciatica [A] *	1/60 (1.67%)	1/63 (1.59%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Somnolence [A] *	1/60 (1.67%)	0/63 (0%)
Syncope [A] *	1/60 (1.67%)	1/63 (1.59%)
Tremor [A] *	1/60 (1.67%)	0/63 (0%)
Vascular dementia [A] *	1/60 (1.67%)	0/63 (0%)
Psychiatric disorders		
Anxiety [A] *	2/60 (3.33%)	3/63 (4.76%)
Confusional state [A] *	1/60 (1.67%)	0/63 (0%)
Depressed mood [A] *	0/60 (0%)	1/63 (1.59%)
Depression [A] *	2/60 (3.33%)	1/63 (1.59%)
Insomnia [A] *	7/60 (11.67%)	8/63 (12.7%)
Restlessness [A] *	0/60 (0%)	1/63 (1.59%)
Renal and urinary disorders		
Dysuria [A] *	1/60 (1.67%)	0/63 (0%)
Haematuria [A] *	1/60 (1.67%)	0/63 (0%)
Haemoglobinuria [A] *	0/60 (0%)	1/63 (1.59%)
Haemorrhage urinary tract [A] *	0/60 (0%)	1/63 (1.59%)
Pollakiuria [A] *	1/60 (1.67%)	0/63 (0%)
Proteinuria [A] *	9/60 (15%)	12/63 (19.05%)
Urinary incontinence [A] *	1/60 (1.67%)	0/63 (0%)
Reproductive system and breast disorders		
Benign prostatic hyperplasia [A] *	0/60 (0%)	1/63 (1.59%)
Perineal pain [A] *	0/60 (0%)	1/63 (1.59%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Vaginal ulceration [A] *	0/60 (0%)	1/63 (1.59%)
Respiratory, thoracic and mediastinal disorders		
Asthma [A] *	0/60 (0%)	1/63 (1.59%)
Chronic obstructive pulmonary disease [A] *	1/60 (1.67%)	0/63 (0%)
Cough [A] *	10/60 (16.67%)	19/63 (30.16%)
Dysphonia [A] *	3/60 (5%)	7/63 (11.11%)
Dyspnoea [A] *	7/60 (11.67%)	11/63 (17.46%)
Dyspnoea exertional [A] *	3/60 (5%)	0/63 (0%)
Epistaxis [A] *	22/60 (36.67%)	9/63 (14.29%)
Haemoptysis [A] *	4/60 (6.67%)	5/63 (7.94%)
Hiccups [A] *	2/60 (3.33%)	2/63 (3.17%)
Nasal congestion [A] *	0/60 (0%)	1/63 (1.59%)
Nasal discomfort [A] *	0/60 (0%)	1/63 (1.59%)
Nasal dryness [A] *	0/60 (0%)	1/63 (1.59%)
Oropharyngeal discomfort [A] *	0/60 (0%)	1/63 (1.59%)
Oropharyngeal pain [A] *	4/60 (6.67%)	8/63 (12.7%)
Pneumothorax [A] *	0/60 (0%)	1/63 (1.59%)
Productive cough [A] *	0/60 (0%)	1/63 (1.59%)
Pulmonary artery thrombosis [A] *	1/60 (1.67%)	0/63 (0%)
Pulmonary embolism [A] *	3/60 (5%)	0/63 (0%)
Pulmonary haemorrhage [A] *	0/60 (0%)	1/63 (1.59%)
Rhinitis allergic [A] *	2/60 (3.33%)	1/63 (1.59%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Rhinorrhoea [A] *	4/60 (6.67%)	3/63 (4.76%)
Sputum increased [A] *	0/60 (0%)	1/63 (1.59%)
Vocal cord atrophy [A] *	1/60 (1.67%)	0/63 (0%)
Wheezing [A] *	0/60 (0%)	1/63 (1.59%)
Skin and subcutaneous tissue disorders		
Acne [A] *	0/60 (0%)	4/63 (6.35%)
Alopecia [A] *	23/60 (38.33%)	12/63 (19.05%)
Dandruff [A] *	0/60 (0%)	1/63 (1.59%)
Decubitus ulcer [A] *	1/60 (1.67%)	1/63 (1.59%)
Dermatitis [A] *	0/60 (0%)	2/63 (3.17%)
Dermatitis acneiform [A] *	0/60 (0%)	2/63 (3.17%)
Dermatitis contact [A] *	2/60 (3.33%)	0/63 (0%)
Dry skin [A] *	1/60 (1.67%)	8/63 (12.7%)
Ecchymosis [A] *	1/60 (1.67%)	0/63 (0%)
Eczema [A] *	0/60 (0%)	1/63 (1.59%)
Hirsutism [A] *	0/60 (0%)	2/63 (3.17%)
Hyperhidrosis [A] *	2/60 (3.33%)	1/63 (1.59%)
Intertrigo [A] *	0/60 (0%)	1/63 (1.59%)
Leukocytoclastic vasculitis [A] *	0/60 (0%)	1/63 (1.59%)
Onychoclasis [A] *	0/60 (0%)	2/63 (3.17%)
Pain of skin [A] *	0/60 (0%)	1/63 (1.59%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Palmar-plantar erythrodysaesthesia syndrome [A] *	0/60 (0%)	4/63 (6.35%)
Petechiae [A] *	1/60 (1.67%)	0/63 (0%)
Pigmentation disorder [A] *	3/60 (5%)	0/63 (0%)
Pruritus [A] *	3/60 (5%)	15/63 (23.81%)
Rash [A] *	9/60 (15%)	39/63 (61.9%)
Rash erythematous [A] *	0/60 (0%)	1/63 (1.59%)
Rash papular [A] *	0/60 (0%)	2/63 (3.17%)
Seborrhoeic dermatitis [A] *	1/60 (1.67%)	0/63 (0%)
Skin erosion [A] *	0/60 (0%)	1/63 (1.59%)
Skin exfoliation [A] *	0/60 (0%)	2/63 (3.17%)
Skin fissures [A] *	0/60 (0%)	1/63 (1.59%)
Skin hyperpigmentation [A] *	0/60 (0%)	1/63 (1.59%)
Skin lesion [A] *	0/60 (0%)	1/63 (1.59%)
Skin toxicity [A] *	0/60 (0%)	1/63 (1.59%)
Skin ulcer [A] *	0/60 (0%)	1/63 (1.59%)
Surgical and medical procedures		
Tooth extraction [A] *	1/60 (1.67%)	0/63 (0%)
Vascular disorders		
Aortic thrombosis [A] *	1/60 (1.67%)	0/63 (0%)
Deep vein thrombosis [A] *	1/60 (1.67%)	0/63 (0%)
Flushing [A] *	0/60 (0%)	1/63 (1.59%)
Haemorrhage [A] *	1/60 (1.67%)	0/63 (0%)

	Bevacizumab + Chemotherapy	Bevacizumab + Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Hypertension [A] *	14/60 (23.33%)	19/63 (30.16%)
Hypotension [A] *	1/60 (1.67%)	0/63 (0%)
Phlebitis [A] *	1/60 (1.67%)	2/63 (3.17%)
Subclavian vein thrombosis [A] *	1/60 (1.67%)	0/63 (0%)
Thrombosis [A] *	0/60 (0%)	1/63 (1.59%)
Varicose vein [A] *	1/60 (1.67%)	0/63 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (11.1)

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.

Results Point of Contact:

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