ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 11/10/2014

A Study of Avastin (Bevacizumab) in Patients With Non-Squamous Non-Small Cell Lung Cancer With Asymptomatic Untreated Brain Metastasis

This study has been completed.

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT00800202

Purpose

This study will assess the efficacy and safety of Avastin combined with first li ne paclitaxel-carboplatin (cohort 1) or second line Tarceva (cohort 2) in patien ts with non-squamous non-small cell lung cancer with asymptomatic untreated brai n metastasis. Two cohorts of patients will be studied; the first will receive Av astin 15mg/kg iv every 3 weeks combined with first line paclitaxel 200mg/m2 iv p lus carboplatin AUC6 iv every 3 weeks for a maximum of 6 cycles, and the second cohort will receive Avastin 15mg/kg iv every 3 weeks combined with second line T arceva 150mg/kg po.The anticipated time on study treatment is until disease prog ression, and the target sample size is 100-500 individuals.

Condition	Intervention	Phase
Non-Small Cell Lung Cancer	Drug: bevacizumab [Avastin] Drug: carboplatin Drug: erlotinib [Tarceva] Drug: paclitaxel	Phase 2

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Non-Randomized, Safety/Efficacy Study
Official Title: An Open Label Study to Assess the Effect of Avastin (Bevacizumab) Combined With First Line Paclitaxel-carboplatin or Second Line Tarceva (Erlotinib) on Progression-free Survival in Non-squamous Non-small Cell Lung Cancer Patients With Asymptomatic Untreated Brain Metastasis

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Percentage of Participants Achieving Progression-Free Survival (PFS) Without Disease Progression or Death at 6 Months [Time Frame: 6 months] [Designated as safety issue: No]

  Tumor progression was defined according to Response Evaluation Criteria In Solid Tumors (RECIST) criteria version 1.1 as increase by at least 20% in the sum of the longest diameters of each target lesion, taking as a reference the smallest sum of the longest diameters, reported since the start of treatment, or appearance of one or more new lesions. PFS (investigator assessed) was defined as the time between the first dose of study treatment and the first event of progression or death by any cause. Participants without an event were censored the last time they were known to be progression free. PFS was analyzed using the Kaplan-Meier method in each treatment arm.
- Percentage of Participants With Disease Progression or Death [Time Frame: Screening, Day 1 of Cycles 3 and 5 and every 2 cycles until end of treatment visit or disease progression or death up to 18 months after enrollment of last participant] [Designated as safety issue: No]

  Tumor progression was defined according to the RECIST criteria as increase by at least 20% in the sum of the longest diameters of each target lesion, taking as a reference the smallest sum of the longest diameters, reported since the start of treatment, or appearance of one or more new lesions. PFS (investigator assessed) was defined as the time between the first dose of study treatment and the first event of progression or death by any cause. Participants without an event were censored the last time they were known to be progression free. PFS was analyzed using the Kaplan-Meier method in each treatment arm.
- Time to Disease Progression or Death [Time Frame: Screening, Day 1 of Cycles 3 and 5 and every 2 cycles until end of treatment visit or disease progression or death up to 18 months after enrollment of last participant] [Designated as safety issue: No]

  Tumor progression was defined as increase by at least 20% in the sum of the longest diameters of each target lesion, taking as a reference the smallest sum of the longest diameters, reported since the start of treatment, or appearance of one or more new lesions. Time to event was determined as the number of months between the first dose of study treatment and the first event of progression or death by any cause. PFS was analyzed using the Kaplan-Meier method in each treatment arm.

Secondary Outcome Measures:

- Percentage of Participants Who Died [Time Frame: Day 1 of Cycles 1, 2, 3, 4, 5, 6 and every 3 weeks up to 18 months or until death] [Designated as safety issue: No]
- Probability of Being Alive at 12 and 18 Months [Time Frame: Months 12 and 18] [Designated as safety issue: No]
- Time to Death [Time Frame: Day 1 of Cycles 1, 2, 3, 4, 5, 6 and every 3 weeks up to 18 months or until death] [Designated as safety issue: No]

  Time to death was determined as the number of months between the first dose of study treatment and the event of death by any cause. Overall survival was analyzed using the Kaplan-Meier method.
- Percentage of Participants Achieving a Best Overall Response of Complete Response or Partial Response as Assessed by the Investigator Using RECIST [Time Frame: Screening, Day 1 of Cycles 3 and 5 and every 2 cycles until end of treatment visit or disease progression or death up to 18 months after enrollment of last participant] [Designated as safety issue: No]

  Overall response defined as best response according to RECIST recorded from date of randomization until disease progression or recurrence. Complete Response (CR): disappearance of all target lesions; Partial response (PR): reduction by at least 30 percent (%) of sum of the longest diameters of each target lesion, taking initial sum of longest diameters as a reference. Participants with a missing response were considered non-responders. 95% CI for one sample binomial using Pearson-Clopper method.

Enrollment: 91
Study Start Date: April 2009
Primary Completion Date: October 2012
Study Completion Date: October 2012

Arms	Assigned Interventions
Experimental: 1	Drug: bevacizumab [Avastin] 15mg/kg iv every 3 weeks Drug: carboplatin AUC6 iv every 3 weeks for 6 cycles Drug: paclitaxel 200mg/m2 iv every 3 weeks for 6 cycles
Experimental: 2	Drug: bevacizumab [Avastin] 15mg/kg iv every 3 weeks Drug: erlotinib [Tarceva] 150mg/day po

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;
- stage IV non-squamous non-small cell lung cancer;
- asymptomatic, untreated brain metastasis;
- ECOG performance status 0-1.

Exclusion Criteria:

- previous treatment for brain metastasis;
- history of migraine or epilepsy;
- previous treatment with angiogenesis inhibitors;
- for cohort 2, previous first line treatment with Avastin or Tarceva;
- current or recent use of aspirin (>325mg/day) or full-dose anticoagulants or thrombolytic agent for therapeutic purposes.

Contacts and Locations

Locations
France
Bordeaux, France, 33076
Brest, France, 29200
Caen, France, 14076

Chartres, France, 28018
Creteil, France, 94010
GAP, France, 05007
Gleize, France, 69400
La Tronche, France, 38700
Lille, France, 59020
Lyon, France, 69317
Marseille, France, 13274
Marseille, France, 13273
Montpellier, France, 34295
Paris, France, 75475
Paris, France, 75970
Paris, France, 75230
Paris, France, 75674
Pierre Benite, France, 69495
Rennes, France, 35033
Saint Herblain, France, 44805
Strasbourg, France, 67065
Toulon, France, 83041
Toulouse, France, 31400
Vandoeuvre Les Nancy, France, 54511
Vandoeuvre-les-nancy, France, 54511
Villejuif, France, 94805

Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party:	Hoffmann-La Roche
Study ID Numbers:	ML21823 2008-006504-33
Health Authority:	France:AFSSAPS

Study Results

Participant Flow

Reporting Groups

	Description
Bevacizumab+Paclitaxel+Carboplatin	Participants received bevacizumab 15 milligrams per kilogram (mg/kg) intravenously (iv) every 3 weeks until progression or unacceptable toxicity along with paclitaxel 200 milligrams per square meter (mg/m^2) iv every 3 weeks for 6 cycles and carboplatin Area Under Curve (AUC) 6.0 milligrams per milliliter per minute (mg/mL/min) iv every 3 weeks for 6 cycles. Bevacizumab was used in addition to standard first line chemotherapy.
Bevacizumab+Erlotinib	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with erlotinib150 milligrams per day (mg/day) administered as tablets orally until progression or unacceptable toxicity. Bevacizumab was used as second-line treatment in addition to erlotinib.

Overall Study

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
Started	67	24
Completed	0	0
Not Completed	67	24
Adverse Event	7	6
Death	1	0
Unspecified	5	0
Disease Progression	54	18

Baseline Characteristics

Analysis Population Description

The Intent-to-Treat (ITT) population: All participants enrolled in each arm who had at least one post-enrollment evaluation. Participants who were lost to follow-up immediately after enrollment were not included in the ITT population.

Reporting Groups

	Description
Bevacizumab+Paclitaxel+Carboplatin	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with paclitaxel 200 mg/m^2 iv every 3 weeks for 6 cycles and carboplatin: AUC 6.0 mg/mL/min iv every 3 weeks for 6 cycles. Bevacizumab was used in addition to standard first line chemotherapy.

	Description
Bevacizumab+Erlotinib	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with erlotinib 150 mg/day administered as tablets orally until progression or unacceptable toxicity. Bevacizumab was used as second-line treatment in addition to erlotinib.

Baseline Measures

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib	Total
Number of Participants	67	24	91
Age, Continuous [units: years] Mean (Standard Deviation)	60.37 (8.31)	54.17 (9.73)	58.74 (9.07)
Gender, Male/Female [units: participants]			
Female	21	13	34
Male	46	11	57

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants Achieving Progression-Free Survival (PFS) Without Disease Progression or Death at 6 Months
Measure Description	Tumor progression was defined according to Response Evaluation Criteria In Solid Tumors (RECIST) criteria version 1.1 as increase by at least 20% in the sum of the longest diameters of each target lesion, taking as a reference the smallest sum of the longest diameters, reported since the start of treatment, or appearance of one or more new lesions. PFS (investigator assessed) was defined as the time between the first dose of study treatment and the first event of progression or death by any cause. Participants without an event were censored the last time they were known to be progression free. PFS was analyzed using the Kaplan-Meier method in each treatment arm.
Time Frame	6 months
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Bevacizumab+Paclitaxel+Carboplatin	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with paclitaxel 200 mg/m^2 iv every 3 weeks for 6 cycles and carboplatin: AUC 6.0 mg/mL/min iv every 3 weeks for 6 cycles. Bevacizumab was used in addition to standard first line chemotherapy.
Bevacizumab+Erlotinib	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with erlotinib 150 mg/day administered as tablets orally until progression or unacceptable toxicity. Bevacizumab was used as second-line treatment in addition to erlotinib.

Measured Values

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
Number of Participants Analyzed	67	24
Percentage of Participants Achieving Progression-Free Survival (PFS) Without Disease Progression or Death at 6 Months [units: percentage of participants] Number (95% Confidence Interval)	56.5 (43.8 to 67.4)	57.2 (37.0 to 76.3)

2. Primary Outcome Measure:

Measure Title	Percentage of Participants With Disease Progression or Death
Measure Description	Tumor progression was defined according to the RECIST criteria as increase by at least 20% in the sum of the longest diameters of each target lesion, taking as a reference the smallest sum of the longest diameters, reported since the start of treatment, or appearance of one or more new lesions. PFS (investigator assessed) was defined as the time between the first dose of study treatment and the first event of progression or death by any cause. Participants without an event were censored the last time they were known to be progression free. PFS was analyzed using the Kaplan-Meier method in each treatment arm.
Time Frame	Screening, Day 1 of Cycles 3 and 5 and every 2 cycles until end of treatment visit or disease progression or death up to 18 months after enrollment of last participant
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Bevacizumab+Paclitaxel+Carboplatin	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with paclitaxel 200 mg/m^2 iv every 3 weeks for 6 cycles and carboplatin: AUC 6.0 mg/mL/min iv every 3 weeks for 6 cycles. Bevacizumab was used in addition to standard first line chemotherapy.
Bevacizumab+Erlotinib	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with erlotinib 150 mg/day administered as tablets orally until progression or unacceptable toxicity. Bevacizumab was used as second-line treatment in addition to erlotinib.

Measured Values

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
Number of Participants Analyzed	67	24
Percentage of Participants With Disease Progression or Death [units: percentage of participants]	89.6	91.7

3. Primary Outcome Measure:

Measure Title	Time to Disease Progression or Death
Measure Description	Tumor progression was defined as increase by at least 20% in the sum of the longest diameters of each target lesion, taking as a reference the smallest sum of the longest diameters, reported since the start of treatment, or appearance of one or more new lesions. Time to event was determined as the number of months between the first dose of study treatment and the first event of progression or death by any cause. PFS was analyzed using the Kaplan-Meier method in each treatment arm.
Time Frame	Screening, Day 1 of Cycles 3 and 5 and every 2 cycles until end of treatment visit or disease progression or death up to 18 months after enrollment of last participant
Safety Issue?	No

Analysis Population Description

ITT Population; only participants with progression or death were included in the analysis.

Reporting Groups

	Description
Bevacizumab+Paclitaxel+Carboplatin	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with paclitaxel 200 mg/m^2 iv every 3 weeks for 6 cycles and carboplatin: AUC 6.0 mg/mL/min iv every 3 weeks for 6 cycles. Bevacizumab was used in addition to standard first line chemotherapy.

	Description
Bevacizumab+Erlotinib	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with erlotinib 150 mg/day administered as tablets orally until progression or unacceptable toxicity. Bevacizumab was used as second-line treatment in addition to erlotinib.

Measured Values

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
Number of Participants Analyzed	60	22
Time to Disease Progression or Death [units: months] Median (95% Confidence Interval)	6.7 (5.7 to 7.1)	6.3 (3.0 to 8.4)

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Died
Measure Description	
Time Frame	Day 1 of Cycles 1, 2, 3, 4, 5, 6 and every 3 weeks up to 18 months or until death
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Bevacizumab+Paclitaxel+Carboplatin	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with paclitaxel 200 mg/m^2 iv every 3 weeks for 6 cycles and carboplatin: AUC 6.0 mg/mL/min iv every 3 weeks for 6 cycles. Bevacizumab was used in addition to standard first line chemotherapy.
Bevacizumab+Erlotinib	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with erlotinib 150 mg/day administered as tablets orally until progression or unacceptable toxicity. Bevacizumab was used as second-line treatment in addition to erlotinib.

Measured Values

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
Number of Participants Analyzed	67	24
Percentage of Participants Who Died	83.6	91.7

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
[units: percentage of participants]		

5. Secondary Outcome Measure:

Measure Title	Probability of Being Alive at 12 and 18 Months
Measure Description	
Time Frame	Months 12 and 18
Safety Issue?	No

Analysis Population Description

ITT Population

Reporting Groups

	Description
Bevacizumab+Paclitaxel+Carboplatin	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with paclitaxel 200 mg/m^2 iv every 3 weeks for 6 cycles and carboplatin: AUC 6.0 mg/mL/min iv every 3 weeks for 6 cycles. Bevacizumab was used in addition to standard first line chemotherapy.
Bevacizumab+Erlotinib	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with erlotinib 150 mg/day administered as tablets orally until progression or unacceptable toxicity. Bevacizumab was used as second-line treatment in addition to erlotinib.

Measured Values

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
Number of Participants Analyzed	67	24
Probability of Being Alive at 12 and 18 Months [units: percent] Number (95% Confidence Interval)		
12 Months	64.2 (51.5 to 74.4)	50.0 (30.5 to 69.5)
18 Months	43.3 (31.3 to 54.7)	41.7 (23.1 to 61.5)

6. Secondary Outcome Measure:

Measure Title	Time to Death

Measure Description	Time to death was determined as the number of months between the first dose of study treatment and the event of death by any cause. Overall survival was analyzed using the Kaplan-Meier method.
Time Frame	Day 1 of Cycles 1, 2, 3, 4, 5, 6 and every 3 weeks up to 18 months or until death
Safety Issue?	No

Analysis Population Description

ITT Population; only participants with an event of death were included in the analysis.

Reporting Groups

	Description
Bevacizumab+Paclitaxel+Carboplatin	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with paclitaxel 200 mg/m^2 iv every 3 weeks for 6 cycles and carboplatin: AUC 6.0 mg/mL/min iv every 3 weeks for 6 cycles. Bevacizumab was used in addition to standard first line chemotherapy.
Bevacizumab+Erlotinib	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with erlotinib 150 mg/day administered as tablets orally until progression or unacceptable toxicity. Bevacizumab was used as second-line treatment in addition to erlotinib.

Measured Values

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
Number of Participants Analyzed	56	22
Time to Death [units: months] Median (95% Confidence Interval)	16.0 (12.0 to 21.0)	12.0 (8.9 to 20.2)

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving a Best Overall Response of Complete Response or Partial Response as Assessed by the Investigator Using RECIST
Measure Description	Overall response defined as best response according to RECIST recorded from date of randomization until disease progression or recurrence. Complete Response (CR): disappearance of all target lesions; Partial response (PR): reduction by at least 30 percent (%) of sum of the longest diameters of each target lesion, taking initial sum of longest diameters as a reference. Participants with a missing response were considered non-responders. 95% CI for one sample binomial using Pearson-Clopper method.
Time Frame	Screening, Day 1 of Cycles 3 and 5 and every 2 cycles until end of treatment visit or disease progression or death up to 18 months after enrollment of last participant
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Bevacizumab+Paclitaxel+Carboplatin	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with paclitaxel 200 mg/m^2 iv every 3 weeks for 6 cycles and carboplatin: AUC 6.0 mg/mL/min iv every 3 weeks for 6 cycles. Bevacizumab was used in addition to standard first line chemotherapy.
Bevacizumab+Erlotinib	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with erlotinib 150 mg/day administered as tablets orally until progression or unacceptable toxicity. Bevacizumab was used as second-line treatment in addition to erlotinib.

Measured Values

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
Number of Participants Analyzed	67	24
Percentage of Participants Achieving a Best Overall Response of Complete Response or Partial Response as Assessed by the Investigator Using RECIST [units: percentage of participants] Number (95% Confidence Interval)	62.7 (50.0 to 74.2)	12.5 (2.7 to 32.4)

Reported Adverse Events

Time Frame	Adverse events were recorded from the date of randomization until end of study or death.
Additional Description	[Not specified]

Reporting Groups

	Description
Bevacizumab+Paclitaxel+Carboplatin	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with paclitaxel 200 mg/m^2 iv every 3 weeks for 6 cycles and carboplatin: AUC 6.0 mg/mL/min iv every 3 weeks for 6 cycles. Bevacizumab was used in addition to standard first line chemotherapy.
Bevacizumab+Erlotinib	Participants received bevacizumab 15 mg/kg iv every 3 weeks until progression or unacceptable toxicity along with erlotinib 150 mg/day administered as tablets orally until progression or unacceptable toxicity. Bevacizumab was used as second-line treatment in addition to erlotinib.

Serious Adverse Events

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Total	27/67 (40.3%)	7/24 (29.17%)
Blood and lymphatic system disorders		
Anaemia [A] *	2/67 (2.99%)	0/24 (0%)
Bicytopenia [A] *	1/67 (1.49%)	0/24 (0%)
Febrile bone marrow aplasia [A] *	2/67 (2.99%)	0/24 (0%)
Febrile neutropenia [A] *	3/67 (4.48%)	0/24 (0%)
Neutropenia [A] *	16/67 (23.88%)	0/24 (0%)
Thrombocytopenia [A] *	1/67 (1.49%)	0/24 (0%)
Cardiac disorders		
Arrhythmia [A] *	1/67 (1.49%)	0/24 (0%)
Gastrointestinal disorders		
Abdominal pain [A] *	0/67 (0%)	1/24 (4.17%)
Abdominal pain upper [A] *	0/67 (0%)	1/24 (4.17%)
Diarrhoea [A] *	1/67 (1.49%)	0/24 (0%)
Oesophageal ulcer [A] *	0/67 (0%)	1/24 (4.17%)
General disorders		
General physical health deterioration [A] *	2/67 (2.99%)	0/24 (0%)
Hyperthermia [A] *	1/67 (1.49%)	0/24 (0%)
Injection site extravasation [A] *	1/67 (1.49%)	0/24 (0%)
Hepatobiliary disorders		
Portal vein thrombosis [A] *	1/67 (1.49%)	0/24 (0%)
Infections and infestations		

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Cellulitis [A] *	1/67 (1.49%)	0/24 (0%)
Staphylococcal sepsis [A] *	0/67 (0%)	1/24 (4.17%)
Urosepsis [A] *	1/67 (1.49%)	0/24 (0%)
Injury, poisoning and procedural complications		
Post procedural haematoma [A] *	0/67 (0%)	1/24 (4.17%)
Metabolism and nutrition disorders		
Hyperkalaemia [A] *	1/67 (1.49%)	0/24 (0%)
Nervous system disorders		
Cerebral haemorrhage [A] *	1/67 (1.49%)	0/24 (0%)
Convulsion [A] *	1/67 (1.49%)	0/24 (0%)
Epilepsy [A] *	1/67 (1.49%)	0/24 (0%)
Hypertensive encephalopathy [A] *	0/67 (0%)	1/24 (4.17%)
Ischaemic stroke [A] *	0/67 (0%)	1/24 (4.17%)
Somnolence [A] *	1/67 (1.49%)	0/24 (0%)
Psychiatric disorders		
Anxiety [A] *	1/67 (1.49%)	0/24 (0%)
Renal and urinary disorders		
Glomerulonephropathy [A] *	1/67 (1.49%)	0/24 (0%)
Haematuria [A] *	0/67 (0%)	1/24 (4.17%)
Proteinuria [A] *	0/67 (0%)	1/24 (4.17%)
Urinary retention [A] *	1/67 (1.49%)	0/24 (0%)
Respiratory, thoracic and mediastinal disorders		
Epistaxis [A] *	0/67 (0%)	1/24 (4.17%)

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Lung disorder [A] *	1/67 (1.49%)	0/24 (0%)
Pulmonary embolism [A] *	2/67 (2.99%)	1/24 (4.17%)
Vascular disorders		
Hypertension [A] *	0/67 (0%)	2/24 (8.33%)
Peripheral artery thrombosis [A] *	1/67 (1.49%)	0/24 (0%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (15.1)

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

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Total	67/67 (100%)	24/24 (100%)
Blood and lymphatic system disorders		
Anaemia [A] *	23/67 (34.33%)	0/24 (0%)
Lymphopenia [A] *	0/67 (0%)	3/24 (12.5%)
Neutropenia [A] *	33/67 (49.25%)	0/24 (0%)
Thrombocytopenia [A] *	23/67 (34.33%)	0/24 (0%)
Gastrointestinal disorders		
Abdominal pain [A] *	0/67 (0%)	3/24 (12.5%)
Constipation [A] *	18/67 (26.87%)	5/24 (20.83%)
Diarrhoea [A] *	18/67 (26.87%)	15/24 (62.5%)
Nausea [A] *	28/67 (41.79%)	6/24 (25%)
Rectal haemorrhage [A] *	0/67 (0%)	3/24 (12.5%)
Vomiting [A] *	17/67 (25.37%)	6/24 (25%)

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
General disorders		
Asthenia [A] *	48/67 (71.64%)	15/24 (62.5%)
Mucosal inflammation [A] *	9/67 (13.43%)	5/24 (20.83%)
Pyrexia [A] *	9/67 (13.43%)	3/24 (12.5%)
Xerosis [A] *	0/67 (0%)	10/24 (41.67%)
Infections and infestations		
Folliculitis [A] *	0/67 (0%)	11/24 (45.83%)
Rhinitis [A] *	9/67 (13.43%)	0/24 (0%)
Investigations		
Weight decreased [A] *	8/67 (11.94%)	4/24 (16.67%)
Metabolism and nutrition disorders		
Decreased appetite [A] *	25/67 (37.31%)	7/24 (29.17%)
Musculoskeletal and connective tissue disorders		
Back pain [A] *	0/67 (0%)	4/24 (16.67%)
Musculoskeletal pain [A] *	9/67 (13.43%)	3/24 (12.5%)
Nervous system disorders		
Dizziness [A] *	7/67 (10.45%)	0/24 (0%)
Headache [A] *	11/67 (16.42%)	8/24 (33.33%)
Neuropathy peripheral [A] *	16/67 (23.88%)	0/24 (0%)
Paraesthesia [A] *	19/67 (28.36%)	0/24 (0%)
Psychiatric disorders		
Insomnia [A] *	0/67 (0%)	3/24 (12.5%)
Renal and urinary disorders		

	Bevacizumab+Paclitaxel+Carboplatin	Bevacizumab+Erlotinib
	Affected/At Risk (%)	Affected/At Risk (%)
Proteinuria [A] *	14/67 (20.9%)	8/24 (33.33%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] *	10/67 (14.93%)	6/24 (25%)
Dysphonia [A] *	0/67 (0%)	5/24 (20.83%)
Epistaxis [A] *	30/67 (44.78%)	10/24 (41.67%)
Skin and subcutaneous tissue disorders		
Alopecia [A] *	29/67 (43.28%)	5/24 (20.83%)
Dermatitis acneiform [A] *	0/67 (0%)	3/24 (12.5%)
Rash [A] *	0/67 (0%)	4/24 (16.67%)
Vascular disorders		
Hypertension [A] *	35/67 (52.24%)	8/24 (33.33%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (15.1)

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.

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