ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 01/22/2015

ClinicalTrials.gov ID: NCT01135498

Study Identification

Unique Protocol ID:	ML19875
Brief Title:	A Study of Avastin (Bevacizumab) in Combination With Xelox and Tarceva in Patients With Metastatic Colorectal Cancer.
Official Title:	An Open-label Study of the Effect of First-line Treatment With Avastin+Xelox, Followed by Avastin+Tarceva, on Progression-free Survival in Patients With Metastatic Colorectal Cancer
Secondary IDs:	

Study Status

Record Verification:	January 2015
Overall Status:	Completed
Study Start:	November 2006
Primary Completion:	April 2010 [Actual]
Study Completion:	April 2010 [Actual]

Sponsor/Collaborators

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

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No

Review Board:	Approval Status: Approved Approval Number: 12/02/2005 Board Name: CEIC DE BURGOS Y SORIA Board Affiliation: Servicio de Salud de la Junta de Castilla y León (SACYL) Phone: 00 34 947 28 16 12 Email:
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Spain: Ministry of Health and Consumption

Study Description

Brief Summary:	This study will evaluate the efficacy and safety of a first-line regimen of Avastin and Xelox (Xeloda + Eloxatin) followed by Avastin and Tarceva, in patients with metastatic colorectal cancer. Patients will receive 6 x 21 day cycles of treatment with Avastin (7.5mg/kg iv on day 1), Xeloda (1000mg/m2 po twice daily on days 1 to 14) and Eloxatin (130mg/m2 iv on day 1). Patients free of disease progression will then continue with Avastin (7.5mg/kg iv once every 3 weeks) and Tarceva (150mg po daily). The anticipated time on study treatment is until disease progression, and the target sample size is <100 individuals.
Detailed Description:	

Conditions

Conditions:	Colorectal Cancer
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 2
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	Non-Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	90 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: bevacizumab [Avastin] Intravenous repeating dose Drug: eloxatin Intravenous repeating dose Drug: capecitabine [Xeloda] Oral repeating dose Drug: erlotinib [Tarceva] Oral repeating dose

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- adult patients, >=18 years of age;
- adenocarcinoma of colon or rectum, with metastatic disease;
- >=1 measurable lesion.

Exclusion Criteria:

- previous treatment with Avastin or Tarceva;
- previous systemic treatment for advanced or metastatic disease;
- adjuvant treatment for non-metastatic disease in past 6 months.

Contacts/Locations

Study Officials: Clinical Trials
Study Chair
Hoffmann-La Roche

Locations: Spain

Jaen, Jaen, Spain, 23007

Terrassa, Barcelona, Spain, 08221

Logroño, La Rioja, Spain, 26006

Lerida, Lerida, Spain, 25198

Santander, Cantabria, Spain, 39008

Zaragoza, Zaragoza, Spain, 50009

Huesca, Huesca, Spain, 22004

Palma de Mallorca, Islas Baleares, Spain, 07198

Teruel, Teruel, Spain, 44002

Burgos, Burgos, Spain, 09006

Sabadell, Barcelona, Barcelona, Spain, 08208

Barakaldo, Vizcaya, Spain, 48903

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Bevacizumab+Oxaliplatin +Capecitabine/Bevacizumab+Erlotinib	Cycles 1-6 (3-week cycles): participants received bevacizumab 7.5 milligrams per kilogram (mg/kg) intravenously (IV) and oxaliplatin 130 mg per square meter (mg/m^2) IV on Day 1 and capecitabine 1000 mg/m^2, tablet, orally (PO), every 12 hours on Days 1 through 14. The cycle was repeated every 21 days for a maximum of 6 cycles. Cycles 7 and beyond (3-week cycles): If all 6 cycles were tolerated with no disease progression, participants then received bevacizumab 7.5 mg/kg IV on Day 1 and erlotinib 150 mg tablets, PO, once daily. This cycle was repeated every 3 weeks until disease progression.

Overall Study

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab+Erlotinib
Started	90
Completed	0
Not Completed	90
Adverse Event	20
Progressive disease	38
Investigator judgement	25
Withdrawal by Subject	4
Death	1
Ongoing at time of analysis	2

Baseline Characteristics

Analysis Population Description

Intent-to-treat (ITT) population: all enrolled participants.

Reporting Groups

	Description
Bevacizumab+Oxaliplatin +Capecitabine/Bevacizumab+Erlotinib	Cycles 1-6 (3-week cycles): participants received bevacizumab 7.5 mg/kg IV and oxaliplatin 130 mg/m^2 IV on Day 1 and capecitabine 1000 mg/m^2, tablet, PO, every 12 hours on Days 1 through 14. The cycle was repeated every 21 days for a maximum of 6 cycles. Cycles 7 and beyond (3-week cycles): If all 6 cycles were tolerated with no disease progression, participants then received bevacizumab 7.5 mg/kg IV on Day 1 and erlotinib 150 mg tablets, PO, once daily. This cycle was repeated every 3 weeks until disease progression.

Baseline Measures

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab+Erlotinib
Number of Participants	90
Age, Continuous [units: years] Mean (Standard Deviation)	59.23 (8.18)
Gender, Male/Female [units: participants]	
Female	29
Male	61

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Disease Progression or Death
Measure Description	Disease progression was defined according to Response Evaluation Criteria in Solid Tumors (RECIST) as a 20 percent (%) increase in the sum of the longest diameter of target lesions, or a measureable increase in a non-target lesion, or the appearance of new lesions.
Time Frame	Start of study to approximately 4 years
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Bevacizumab+Oxaliplatin +Capecitabine/Bevacizumab+Erlotinib	Cycles 1-6 (3-week cycles): participants received bevacizumab 7.5 mg/kg IV and oxaliplatin 130 mg/m^2 IV on Day 1 and capecitabine 1000 mg/m^2, tablet, PO, every 12 hours on Days 1 through 14. The cycle was repeated every 21 days for a maximum of 6 cycles. Cycles 7 and beyond (3-week cycles): If all 6 cycles were tolerated with no disease progression, participants then received bevacizumab 7.5 mg/kg IV on Day 1 and erlotinib 150 mg tablets, PO, once daily. This cycle was repeated every 3 weeks until disease progression.

Measured Values

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab+Erlotinib
Number of Participants Analyzed	90
Percentage of Participants With Disease Progression or Death [units: percentage of participants]	61.1

2. Primary Outcome Measure:

Measure Title	Progression-Free Survival
Measure Description	Progression-free survival was defined as the time from the date of informed consent until the date when the participant had progression of disease or died from disease progression. Participants who received surgical treatment after treatment ended were censored at the time of surgery. Participants who left the study for reasons other than progression of the disease were censored on the date on which they received a later antitumor therapy (with the same or different drugs, radiotherapy, or surgery).
Time Frame	From study start up to approximately 4 years
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Bevacizumab+Oxaliplatin +Capecitabine/Bevacizumab+Erlotinib	Cycles 1-6 (3-week cycles): participants received bevacizumab 7.5 mg/kg IV and oxaliplatin 130 mg/m^2 IV on Day 1 and capecitabine 1000 mg/m^2, tablet, PO, every 12 hours on Days 1 through 14. The cycle was repeated every 21 days for a maximum of 6 cycles. Cycles 7 and beyond (3-week cycles): If all 6 cycles were tolerated with no disease progression, participants then received bevacizumab 7.5 mg/kg IV on Day 1 and erlotinib 150 mg tablets, PO, once daily. This cycle was repeated every 3 weeks until disease progression.

Measured Values

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab+Erlotinib
Number of Participants Analyzed	90
Progression-Free Survival [units: months] Median (95% Confidence Interval)	9.18 (7.86 to 11.87)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving Objective Response (Complete Response [CR] or Partial Response [PR])
Measure Description	Percentage of participants with objective response based assessment of CR or PR according to Response Evaluation Criteria in Solid Tumors (RECIST). CR was defined as complete disappearance of all target lesions and non-target disease, with the exception of nodal disease. All nodes, both target and non-target, must have decreased to normal (short axis less than [<]10 millimeters [mm]) and no new lesions. PR was defined as greater than or equal to (≥)30 percent (%) decrease under baseline of the sum of diameters of all target lesions. The short axis was used in the sum for target nodes, while the longest diameter was used in the sum for all other target lesions. No unequivocal progression of non-target disease. No new lesions.
Time Frame	From study start up to approximately 4 years
Safety Issue?	No

Analysis Population Description

Response-Evaluable population: all enrolled participants who received at least 3 cycles of treatment, had all baseline lesions evaluated at least once after receiving the third cycle (using same technique as at baseline), and were without major violations of the study protocol.

Reporting Groups

	Description
Bevacizumab+Oxaliplatin +Capecitabine/Bevacizumab+Erlotinib	Cycles 1-6 (3-week cycles): participants received bevacizumab 7.5 mg/kg IV and oxaliplatin 130 mg/m^2 IV on Day 1 and capecitabine 1000 mg/m^2, tablet, PO, every 12 hours on Days 1 through 14. The cycle was repeated every 21 days for a maximum of 6 cycles. Cycles 7 and beyond (3-week cycles): If all 6 cycles were tolerated with no disease progression, participants then received bevacizumab 7.5 mg/kg IV on Day 1 and erlotinib 150 mg tablets, PO, once daily. This cycle was repeated every 3 weeks until disease progression.

Measured Values

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab+Erlotinib
Number of Participants Analyzed	84
Percentage of Participants Achieving Objective Response (Complete Response [CR] or Partial Response [PR]) [units: percentage of participants]	55.95

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants Achieving Disease Control (CR, PR, or No Change [NC])
Measure Description	Percent of participants with confirmed CR, PR, or NC. Per RECIST version (v)1.0: CR was defined as disappearance of all target and non-target lesions. PR was defined as ≥30% decrease in sum of longest diameters of target lesions taking as reference baseline sum longest diameters associated to non-progressive disease response for non-target lesions. NC was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease taking as reference smallest sum of longest dimensions since treatment started associated to non-progressive disease response for non-target lesions.
Time Frame	From study start up to approximately 4 years
Safety Issue?	No

Analysis Population Description

Response-Evaluable population

Reporting Groups

	Description
Bevacizumab+Oxaliplatin +Capecitabine/Bevacizumab+Erlotinib	Cycles 1-6 (3-week cycles): participants received bevacizumab 7.5 mg/kg IV and oxaliplatin 130 mg/m^2 IV on Day 1 and capecitabine 1000 mg/m^2, tablet, PO, every 12 hours on Days 1 through 14. The cycle was repeated every 21 days for a maximum of 6 cycles. Cycles 7 and beyond (3-week cycles): If all 6 cycles were tolerated with no disease progression, participants then received bevacizumab 7.5 mg/kg IV on Day 1 and erlotinib 150 mg tablets, PO, once daily. This cycle was repeated every 3 weeks until disease progression.

Measured Values

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab+Erlotinib
Number of Participants Analyzed	84
Percentage of Participants Achieving Disease Control (CR, PR, or No Change [NC]) [units: percentage of participants]	92.86

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Died
Measure Description	
Time Frame	From study start up to approximately 4 years
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Bevacizumab+Oxaliplatin +Capecitabine/Bevacizumab+Erlotinib	ACycles 1-6 (3-week cycles): participants received bevacizumab 7.5 mg/kg IV and oxaliplatin 130 mg/m^2 IV on Day 1 and capecitabine 1000 mg/m^2, tablet, PO, every 12 hours on Days 1 through 14. The cycle was repeated every 21 days for a maximum of 6 cycles. Cycles 7 and beyond (3-week cycles): If all 6 cycles were tolerated with no disease progression, participants then received bevacizumab 7.5 mg/kg IV on Day 1 and erlotinib 150 mg tablets, PO, once daily. This cycle was repeated every 3 weeks until disease progression.

Measured Values

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab+Erlotinib
Number of Participants Analyzed	90
Percentage of Participants Who Died [units: percentage of participants]	58.89

6. Secondary Outcome Measure:

Measure Title	Overall Survival (OS)
Measure Description	Overall survival was defined as the time from the date of informed consent to the date of death (regardless of the cause of death). There was no restriction; survival was calculated until the date of death, even if another line of treatment was received, or until the date censored (last contact with the participant even if drugs different from the study treatment schedule were received). For all participants, survival information was collected until the date of death, the last contact, or the last follow-up.
Time Frame	From study start up to approximately 4 years
Safety Issue?	No

Analysis Population Description

ITT population

Reporting Groups

	Description
Bevacizumab+Oxaliplatin +Capecitabine/Bevacizumab+Erlotinib	Cycles 1-6 (3-week cycles): participants received bevacizumab 7.5 mg/kg IV and oxaliplatin 130 mg/m^2 IV on Day 1 and capecitabine 1000 mg/m^2, tablet, PO, every 12 hours on Days 1 through 14. The cycle was repeated every 21 days for a maximum of 6 cycles. Cycles 7 and beyond (3-week cycles): If all 6 cycles were tolerated with no disease progression, participants then received bevacizumab 7.5 mg/kg IV on Day 1 and erlotinib 150 mg tablets, PO, once daily. This cycle was repeated every 3 weeks until disease progression.

Measured Values

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab+Erlotinib
Number of Participants Analyzed	90
Overall Survival (OS) [units: months] Median (95% Confidence Interval)	25.79 (17.99 to 30.92)

Reported Adverse Events

Time Frame	Participants were monitored for adverse events (AEs) from the first dose of study drug until the end of the study.
Additional Description	An AE was defined as any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A separate analysis of nonserious AEs was not performed, therefore the AE section includes all AEs reported during the study, not just nonserious events.

Reporting Groups

	Description
Bevacizumab+Eloxatin+Capecitabine/ Bevacizumab+Erlotinib	A cycle was defined as the following: participants received 7.5 mg/kg bevacizumab, IV on Day 1; 130 mg/m^2 eloxatin tablets, orally, on Days 1 through 14; and 1000 mg/m^2 capecitabine tablets, orally, every 12 hours on Days 1 through 14. The cycle was repeated every 21 days for a maximum of 6 cycles. If all 6 cycles were tolerated with no disease progression, participants then received 7.5 mg/kg bevacizumab, IV on Day 1 and 150 mg erlotinib tablets, orally, once daily. This cycle was repeated every 3 weeks until disease progression.

Serious Adverse Events

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Total	33/90 (36.67%)
Blood and lymphatic system disorders	
Anaemia [A] *	2/90 (2.22%)
Leukopenia [A] *	1/90 (1.11%)
Neutropenia [A] *	7/90 (7.78%)
Cardiac disorders	
Myocardial ischaemia [A] *	1/90 (1.11%)
Gastrointestinal disorders	
Abdominal distension [A] *	1/90 (1.11%)
Abdominal pain [A] *	2/90 (2.22%)

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Abdominal pain upper [A] *	1/90 (1.11%)
Colitis ischaemic [A] *	1/90 (1.11%)
Diarrhoea [A] *	18/90 (20%)
Enteritis [A] *	1/90 (1.11%)
Enterocutaneous fistula [A] *	1/90 (1.11%)
Intestinal obstruction [A] *	1/90 (1.11%)
Large intestine perforation [A] *	1/90 (1.11%)
Nausea [A] *	2/90 (2.22%)
Rectal haemorrhage [A] *	1/90 (1.11%)
Subileus [A] *	1/90 (1.11%)
Upper gastrointestinal haemorrhage [A] *	1/90 (1.11%)
Vomiting [A] *	4/90 (4.44%)
General disorders	
Adverse drug reaction [A] *	1/90 (1.11%)
Asthenia [A] *	11/90 (12.22%)
General physical health deterioration [A] *	2/90 (2.22%)
Mucosal inflammation [A] *	2/90 (2.22%)
Pyrexia [A] *	1/90 (1.11%)
Hepatobiliary disorders	
Hepatotoxicity [A] *	1/90 (1.11%)
Jaundice cholestatic [A] *	1/90 (1.11%)
Immune system disorders	

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Drug hypersensitivity [A] *	1/90 (1.11%)
Infections and infestations	
Folliculitis [A] *	1/90 (1.11%)
Gastroenteritis [A] *	1/90 (1.11%)
Infection [A] *	2/90 (2.22%)
Perirectal abscess [A] *	1/90 (1.11%)
Pneumonia [A] *	1/90 (1.11%)
Respiratory tract infection [A] *	1/90 (1.11%)
Urinary tract infection [A] *	1/90 (1.11%)
Injury, poisoning and procedural complications	
Seroma [A] *	1/90 (1.11%)
Investigations	
Blood potassium decreased [A] *	1/90 (1.11%)
Gamma-glutamyltransferase [A] *	2/90 (2.22%)
Metabolism and nutrition disorders	
Anorexia [A] *	1/90 (1.11%)
Dehydration [A] *	1/90 (1.11%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Tumour perforation [A] *	1/90 (1.11%)
Nervous system disorders	
Dysaesthesia [A] *	1/90 (1.11%)
Headache [A] *	1/90 (1.11%)
Psychiatric disorders	

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Anxiety [A] *	2/90 (2.22%)
Confusional state [A] *	1/90 (1.11%)
Renal and urinary disorders	
Acute prerenal failure [A] *	1/90 (1.11%)
Hydronephrosis [A] *	1/90 (1.11%)
Ureteric obstruction [A] *	1/90 (1.11%)
Respiratory, thoracic and mediastinal disorders	
Pulmonary embolism [A] *	3/90 (3.33%)
Skin and subcutaneous tissue disorders	
Acne [A] *	3/90 (3.33%)
Erythema [A] *	1/90 (1.11%)
Palmar-plantar erythrodysaesthesia [A] *	1/90 (1.11%)
Rash [A] *	6/90 (6.67%)
Skin reaction [A] *	1/90 (1.11%)
Skin toxicity [A] *	1/90 (1.11%)
Toxic skin eruption [A] *	1/90 (1.11%)
Vascular disorders	
Deep vein thrombosis [A] *	3/90 (3.33%)
Hypertension [A] *	4/90 (4.44%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (8.1)

Other Adverse Events

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

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Total	89/90 (98.89%)
Blood and lymphatic system disorders	
Anaemia [A] *	18/90 (20%)
Febrile neutropenia [A] *	1/90 (1.11%)
Leukopenia [A] *	12/90 (13.33%)
Neutropenia [A] *	25/90 (27.78%)
Neutrophilia [A] *	1/90 (1.11%)
Thrombocythaemia [A] *	1/90 (1.11%)
Thrombocytopenia [A] *	13/90 (14.44%)
Cardiac disorders	
Myocardial ischaemia [A] *	1/90 (1.11%)
Tachycardia [A] *	1/90 (1.11%)
Ear and labyrinth disorders	
Vertigo [A] *	2/90 (2.22%)
Eye disorders	
Conjunctival haemorrhage [A] *	1/90 (1.11%)
Conjunctivitis [A] *	3/90 (3.33%)
Lacrimation increased [A] *	2/90 (2.22%)
Ocular icterus [A] *	1/90 (1.11%)
Scotoma [A] *	1/90 (1.11%)
Xerophthalmia [A] *	1/90 (1.11%)
Gastrointestinal disorders	

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Abdominal discomfort [A] *	2/90 (2.22%)
Abdominal distension [A] *	2/90 (2.22%)
Abdominal pain [A] *	31/90 (34.44%)
Abdominal pain lower [A] *	1/90 (1.11%)
Abdominal pain upper [A] *	9/90 (10%)
Aerophagia [A] *	1/90 (1.11%)
Anal discomfort [A] *	1/90 (1.11%)
Anal ulcer [A] *	1/90 (1.11%)
Atrophy of tongue papillae [A] *	1/90 (1.11%)
Colitis ischaemic [A] *	1/90 (1.11%)
Constipation [A] *	16/90 (17.78%)
Diarrhoea [A] *	56/90 (62.22%)
Dry mouth [A] *	3/90 (3.33%)
Dyspepsia [A] *	1/90 (1.11%)
Dysphagia [A] *	1/90 (1.11%)
Enteritis [A] *	1/90 (1.11%)
Enterocutaneous fistula [A] *	1/90 (1.11%)
Epigastric discomfort [A] *	2/90 (2.22%)
Flatulence [A] *	2/90 (2.22%)
Gastrointestinal mucositis [A] *	1/90 (1.11%)
Gingival bleeding [A] *	6/90 (6.67%)
Haematochezia [A] *	1/90 (1.11%)

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Haemorrhoids [A] *	1/90 (1.11%)
Intestinal obstruction [A] *	1/90 (1.11%)
Large intestine perforation [A] *	1/90 (1.11%)
Lip ulceration [A] *	1/90 (1.11%)
Nausea [A] *	41/90 (45.56%)
Odynophagia [A] *	4/90 (4.44%)
Pancreatitis acute [A] *	1/90 (1.11%)
Proctalgia [A] *	2/90 (2.22%)
Rectal haemorrhage [A] *	9/90 (10%)
Rectal tenesmus [A] *	4/90 (4.44%)
Stomatitis [A] *	12/90 (13.33%)
Subileus [A] *	2/90 (2.22%)
Toothache [A] *	1/90 (1.11%)
Upper gastrointestinal haemorrhage [A] *	1/90 (1.11%)
Vomiting [A] *	36/90 (40%)
General disorders	
Adverse drug reaction [A] *	1/90 (1.11%)
Asthenia [A] *	69/90 (76.67%)
Face oedema [A] *	1/90 (1.11%)
General physical health deterioration [A] *	2/90 (2.22%)
Hernia [A] *	1/90 (1.11%)
Infusion site pain [A] *	1/90 (1.11%)

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Mucosal dryness [A] *	1/90 (1.11%)
Mucosal inflammation [A] *	18/90 (20%)
Oedema [A] *	3/90 (3.33%)
Oedema peripheral [A] *	3/90 (3.33%)
Pain [A] *	3/90 (3.33%)
Pyrexia [A] *	21/90 (23.33%)
Temperature intolerance [A] *	1/90 (1.11%)
Hepatobiliary disorders	
Hepatic pain [A] *	1/90 (1.11%)
Hepatomegaly [A] *	2/90 (2.22%)
Hepatotoxicity [A] *	1/90 (1.11%)
Jaundice [A] *	1/90 (1.11%)
Jaundice cholestatic [A] *	1/90 (1.11%)
Immune system disorders	
Drug hypersensitivity [A] *	3/90 (3.33%)
Hypersensitivity [A] *	3/90 (3.33%)
Infections and infestations	
Abscess limb [A] *	1/90 (1.11%)
Cellulitis [A] *	4/90 (4.44%)
Ear infection [A] *	1/90 (1.11%)
Escherichia urinary tract infection [A] *	1/90 (1.11%)
Folliculitis [A] *	4/90 (4.44%)

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Furuncle [A] *	1/90 (1.11%)
Gastroenteritis [A] *	1/90 (1.11%)
Infection [A] *	4/90 (4.44%)
Influenza [A] *	1/90 (1.11%)
Nail infection [A] *	1/90 (1.11%)
Nasopharyngitis [A] *	3/90 (3.33%)
Oral infection [A] *	3/90 (3.33%)
Paronychia [A] *	1/90 (1.11%)
Perirectal abscess [A] *	1/90 (1.11%)
Pharyngitis [A] *	1/90 (1.11%)
Pneumonia [A] *	1/90 (1.11%)
Respiratory tract infection [A] *	4/90 (4.44%)
Skin infection [A] *	1/90 (1.11%)
Subcutaneous abscess [A] *	1/90 (1.11%)
Upper respiratory tract infection [A] *	1/90 (1.11%)
Urinary tract infection [A] *	3/90 (3.33%)
Injury, poisoning and procedural complications	
Contusion [A] *	1/90 (1.11%)
Fall [A] *	1/90 (1.11%)
Hand fracture [A] *	1/90 (1.11%)
Injury [A] *	1/90 (1.11%)
Seroma [A] *	1/90 (1.11%)

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Investigations	
Alanine aminotransferase [A] *	1/90 (1.11%)
Alanine aminotransferase increased [A] *	2/90 (2.22%)
Aspartate aminotransferase increased [A] *	4/90 (4.44%)
Blood alkaline phosphatase increased [A] *	2/90 (2.22%)
Blood bilirubin increased [A] *	1/90 (1.11%)
Blood glucose abnormal [A] *	1/90 (1.11%)
Blood lactate dehydrogenase [A] *	2/90 (2.22%)
Blood lactate dehydrogenase increased [A] *	1/90 (1.11%)
Blood potassium decreased [A] *	2/90 (2.22%)
Gamma-glutamyltransferase [A] *	4/90 (4.44%)
Platelet count decreased [A] *	1/90 (1.11%)
Weight decreased [A] *	5/90 (5.56%)
Weight increased [A] *	1/90 (1.11%)
Metabolism and nutrition disorders	
Anorexia [A] *	35/90 (38.89%)
Decreased appetite [A] *	8/90 (8.89%)
Dehydration [A] *	1/90 (1.11%)
Hyperglycaemia [A] *	1/90 (1.11%)
Hyperuricaemia [A] *	1/90 (1.11%)
Hypoglycaemia [A] *	1/90 (1.11%)
Hypomagnesaemia [A] *	1/90 (1.11%)

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Musculoskeletal and connective tissue disorders	
Arthralgia [A] *	4/90 (4.44%)
Back pain [A] *	8/90 (8.89%)
Bone pain [A] *	4/90 (4.44%)
Buttock pain [A] *	1/90 (1.11%)
Chest wall pain [A] *	1/90 (1.11%)
Groin pain [A] *	1/90 (1.11%)
Muscle contracture [A] *	1/90 (1.11%)
Muscle tightness [A] *	2/90 (2.22%)
Musculoskeletal pain [A] *	2/90 (2.22%)
Myalgia [A] *	3/90 (3.33%)
Neck pain [A] *	1/90 (1.11%)
Osteoarthritis [A] *	2/90 (2.22%)
Pain in extremity [A] *	6/90 (6.67%)
Shoulder pain [A] *	2/90 (2.22%)
Trismus [A] *	1/90 (1.11%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
Cancer pain [A] *	2/90 (2.22%)
Tumour perforation [A] *	1/90 (1.11%)
Nervous system disorders	
Ageusia [A] *	1/90 (1.11%)
Aphonia [A] *	1/90 (1.11%)

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Dizziness [A] *	1/90 (1.11%)
Dysaesthesia [A] *	24/90 (26.67%)
Dysgeusia [A] *	8/90 (8.89%)
Headache [A] *	7/90 (7.78%)
Hypoaesthesia [A] *	1/90 (1.11%)
Neuropathy [A] *	4/90 (4.44%)
Neurotoxicity [A] *	32/90 (35.56%)
Paraesthesia [A] *	35/90 (38.89%)
Parosmia [A] *	1/90 (1.11%)
Somnolence [A] *	1/90 (1.11%)
Tremor [A] *	1/90 (1.11%)
Psychiatric disorders	
Anxiety [A] *	5/90 (5.56%)
Confusional state [A] *	1/90 (1.11%)
Depression [A] *	2/90 (2.22%)
Insomnia [A] *	6/90 (6.67%)
Renal and urinary disorders	
Acute prerenal failure [A] *	1/90 (1.11%)
Dysuria [A] *	2/90 (2.22%)
Hydronephrosis [A] *	1/90 (1.11%)
Proteinuria [A] *	9/90 (10%)
Renal colic [A] *	1/90 (1.11%)

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Renal failure [A] *	1/90 (1.11%)
Ureteric obstruction [A] *	1/90 (1.11%)
Urinary incontinence [A] *	1/90 (1.11%)
Reproductive system and breast disorders	
Amenorrhoea [A] *	2/90 (2.22%)
Perineal pain [A] *	1/90 (1.11%)
Respiratory, thoracic and mediastinal disorders	
Cough [A] *	5/90 (5.56%)
Dysphonia [A] *	4/90 (4.44%)
Dyspnoea [A] *	4/90 (4.44%)
Epistaxis [A] *	14/90 (15.56%)
Haemoptysis [A] *	1/90 (1.11%)
Hiccups [A] *	3/90 (3.33%)
Laryngospasm [A] *	2/90 (2.22%)
Nasal congestion [A] *	1/90 (1.11%)
Pharyngeal erythema [A] *	1/90 (1.11%)
Pharyngolaryngeal pain [A] *	1/90 (1.11%)
Pulmonary embolism [A] *	3/90 (3.33%)
Rhinorrhoea [A] *	4/90 (4.44%)
Skin and subcutaneous tissue disorders	
Acanthosis [A] *	1/90 (1.11%)
Acne [A] *	8/90 (8.89%)

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Alopecia [A] *	1/90 (1.11%)
Dermatitis [A] *	2/90 (2.22%)
Dry skin [A] *	5/90 (5.56%)
Erythema [A] *	5/90 (5.56%)
Leukocytoclastic vasculitis [A] *	1/90 (1.11%)
Nail disorder [A] *	2/90 (2.22%)
Nail dystrophy [A] *	1/90 (1.11%)
Night sweats [A] *	1/90 (1.11%)
Onycholysis [A] *	1/90 (1.11%)
Palmar-plantar erythrodysaesthesia syndrome [A] *	29/90 (32.22%)
Plantar erythema [A] *	1/90 (1.11%)
Pruritus [A] *	3/90 (3.33%)
Rash [A] *	38/90 (42.22%)
Skin fissures [A] *	2/90 (2.22%)
Skin hyperpigmentation [A] *	2/90 (2.22%)
Skin reaction [A] *	4/90 (4.44%)
Skin toxicity [A] *	2/90 (2.22%)
Subcutaneous nodule [A] *	1/90 (1.11%)
Toxic skin eruption [A] *	1/90 (1.11%)
Vascular disorders	
Deep vein thrombosis [A] *	3/90 (3.33%)

	Bevacizumab+Eloxatin+Capecitabine/Bevacizumab+Erlotinib
	Affected/At Risk (%)
Hypertension [A] *	15/90 (16.67%)
Hypertensive crisis [A] *	1/90 (1.11%)
Hypotension [A] *	1/90 (1.11%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (8.1)

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 the Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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