ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 12/08/2014

ClinicalTrials.gov ID: NCT01077739

Study Identification

Unique Protocol ID:	ML22519
Brief Title:	A Study of Avastin (Bevacizumab) With XELOX or FOLFOX in Patients With Metastatic Colorectal Cancer and Disease Progression Under First-line FOLFIRI and Avastin
Official Title:	A Single-arm Open-label Phase II Study: Treatment Beyond Progression by Adding Bevacizumab to XELOX or FOLFOX Chemotherapy in Patients With Metastatic Colorectal Cancer and Disease Progression Under First-line FOLFIRI + Bevacizumab Combination
Secondary IDs:	2009-012090-36

Study Status

Record Verification:	December 2014
Overall Status:	Completed
Study Start:	July 2009
Primary Completion:	January 2012 [Actual]
Study Completion:	January 2012 [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: 2009/208 Board Name: Commissie voor Medische Ethiek UZ Gent Board Affiliation: Universitair Ziekenhuis Gent Phone: +3293325613 Email: ethisch.comitte@ugent.be
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Belgium: Federal Agency for Medicines and Health Products, FAMHP

Study Description

Brief Summary:	This open-label single arm study will evaluate the efficacy and safety of Avastin added to XELOX or FOLFOX in patients with metastatic colorectal cancer and disease progression on 1st line therapy with FOLFIRI plus Avastin. Patients will receive either Avastin (7.5mg/kg iv infusion every 3 weeks) and standard XELOX (Xeloda [capecitabine] plus oxaliplatin) chemotherapy or Avastin (5 mg/kg iv infusion every 2 weeks) and standard FOLFOX (5-FU and leucovorin plus oxaliplatin) chemotherapy. 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:	Parallel Assignment
Number of Arms:	1

Masking:	Open Label
Allocation:	Non-Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	75 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Avastin (bevacizumab) + standard of care	Drug: fluorouracil (5FU) standard FOLFOX regimen Drug: leucovorin standard FOLFOX regimen Drug: bevacizumab [Avastin] 7.5 mg/kg iv infusion every 3 weeks OR 5 mg/kg iv infusion every 2 weeks Drug: capecitabine [Xeloda] standard XELOX regimen Drug: oxaliplatin standard XELOX or FOLFOX regimen

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
- metastatic colorectal cancer
- at least 1 measurable lesion according to RECIST v. 1.1
- patients with disease progression with prior FOLFIRI + Avastin therapy who are not candidates for primary metastasectomy
- disease progression </= 8 weeks after last dose of Avastin
- ECOG </=2
- No more than 8 weeks between 1st-line treatment with FOLFIRI + Avastin and 2nd-line treatment with XELOX or FOLFOX + Avastin

Exclusion Criteria:

- disease progression > 8 weeks after last Avastin administration
- clinically significant cardiovascular disease
- CNS disease except for treated brain metastasis
- history of other malignancies within 2 years prior to start of study treatment (with the exception of curatively treated basal and squamous cell carcinoma of the skin or in situ carcinoma of the cervix)
- major surgery, open biopsy, or significant traumatic injury within 28 days prior to start of study treatment

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Belgium

Gent, Belgium, 9000

AYE, Belgium, 6900

Mechelen, Belgium, 2800

Arlon, Belgium, 6700

Bruxelles, Belgium, 1180

Charleroi, Belgium, 6000

Montigny-le-Tilleul, Belgium, 6110

Bruxelles, Belgium, 1020

Genk, Belgium, 3600

Dendermonde, Belgium, 9200

Brugge, Belgium, 8000

Hasselt, Belgium, 3500

Brasschaat, Belgium, 2930

Namur, Belgium, 5000

Kortrijk, Belgium, 8500

Merksem, Belgium, 2170

Gent, Belgium, 9000

Aalst, Belgium, 9300

Wilrijk, Belgium, 2610

Bruxelles, Belgium, 1200

Mont-godinne, Belgium, 5530

Verviers, Belgium, 4800

Gent, Belgium, 9000

Sint-Niklaas, Belgium, 9100

Oostende, Belgium, 8400

Bonheiden, Belgium, 2820

Edegem, Belgium, 2650

Assebroek, Belgium, 8310

Aalst, Belgium, 9300

Tournai, Belgium, 7500

Turnhout, Belgium, 2300

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Bevacizumab + Oxaliplatin + Capecitabine	Participants received bevacizumab 7.5 milligrams per kilogram (mg/kg) intravenously (IV) on Day 1; oxaliplatin 130 mg per square meter (mg/m^2) IV on Day 1; and capecitabine 1000 mg/m^2, orally (PO), twice daily (BID) on Days 1 through 14 (followed by 1-week rest period). The cycle was repeated every 3 weeks until disease progression.
Bevacizumab + 5-fluorouracil/ Oxaliplatin/Leucovorin (FOLFOX)	Participants received bevacizumab 5.0 mg/kg IV on Day 1 and FOLFOX (5-fluorouracil [5-FU] plus leucovorin and oxaliplatin) administered on Days 1 and 2 (followed by a rest period on Days 3 through 14); the specific FOLFOX regimen was determined on an individual participant basis by the investigator (5-FU and leucovorin dose was dependent on choice of FOLFOX regimen; oxaliplatin was administered at a dose ranging from 85 to 130 mg/m^2 IV on Day 1 based on choice of FOLFOX regimen). The cycle was repeated every 2 weeks until disease progression.

Overall Study

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + 5-fluorouracil/ Oxaliplatin/Leucovorin (FOLFOX)
Started	25	50
Completed	20	40
Not Completed	5	10
Premature withdrawal	1	3
Withdrawal by Subject	1	0
Death	0	3
Unacceptable toxicity	1	2
Not specified	2	2

Baseline Characteristics

Analysis Population Description

Intent-to-treat (ITT) population: all enrolled participants who received at least 1 dose of the investigational and non-investigational products.

Reporting Groups

	Description
Bevacizumab + Oxaliplatin + Capecitabine	Participants received bevacizumab 7.5 mg/kg IV on Day 1; oxaliplatin 130 mg/m^2 IV on Day 1; and capecitabine 1000 mg/m^2, PO, BID on Days 1 through 14 (followed by 1-week rest period). The cycle was repeated every 3 weeks until disease progression.
Bevacizumab + FOLFOX	Participants received bevacizumab 5.0 mg/kg IV on Day 1 and FOLFOX (5-FU plus leucovorin and oxaliplatin) administered on Days 1 and 2 (followed by a rest period on Days 3 through 14); the specific FOLFOX regimen was determined on an individual participant basis by the investigator (5-FU and leucovorin dose was dependent on choice of FOLFOX regimen; oxaliplatin was administered at a dose ranging from 85 to 130 mg/m^2 IV on Day 1 based on choice of FOLFOX regimen). The cycle was repeated every 2 weeks until disease progression.

Baseline Measures

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX	Total
Number of Participants	25	50	75
Age, Continuous [units: years] Mean (Standard Deviation)	59.6 (8.9)	64.9 (8.7)	63.1 (9.0)
Gender, Male/Female [units: participants]			
Female	8	21	29
Male	17	29	46

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Progression-Free Survival (PFS) From the Start of Treatment Beyond Progression
Measure Description	PFS from the start of treatment beyond progression was defined as the interval between the start of beyond-progression therapy and the date at which disease progression was documented. Progression of disease was evaluated using Response Evaluation Criteria in Solid Tumors (RECIST) criteria version 1.1 and abdominal/pelvic computerized tomography (CT) or magnetic resonance imaging (MRI) scanning as a 20% increase in the sum of the longest diameter of target lesions, or a measurable increase in a non-target lesion, or the appearance of new lesions. The same method of assessment and the same technique were to be used to evaluate each lesion throughout the entire study. If more than one method was used, data from the most accurate method according to RECIST were recorded. Median PFS was estimated using the Kaplan-Meier method.
Time Frame	Baseline, every 9 weeks until disease progression, at end of treatment or withdrawal, for up to 24 months
Safety Issue?	No

Analysis Population Description
ITT population

Reporting Groups

	Description
Bevacizumab + Oxaliplatin + Capecitabine	Participants received bevacizumab 7.5 mg/kg IV on Day 1; oxaliplatin 130 mg/m^2 IV on Day 1; and capecitabine 1000 mg/m^2, PO, BID on Days 1 through 14 (followed by 1-week rest period). The cycle was repeated every 3 weeks until disease progression.
Bevacizumab + FOLFOX	Participants received bevacizumab 5.0 mg/kg IV on Day 1 and FOLFOX (5-FU plus leucovorin and oxaliplatin) administered on Days 1 and 2 (followed by a rest period on Days 3 through 14); the specific FOLFOX regimen was determined on an individual participant basis by the investigator (5-FU and leucovorin dose was dependent on choice of FOLFOX regimen; oxaliplatin was administered at a dose ranging from 85 to 130 mg/m^2 IV on Day 1 based on choice of FOLFOX regimen). The cycle was repeated every 2 weeks until disease progression.

Measured Values

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
Number of Participants Analyzed	25	50
Progression-Free Survival (PFS) From the Start of Treatment Beyond Progression [units: months] Median (95% Confidence Interval)	6.3 (4.1 to 7.6)	5.1 (3.8 to 6.0)

2. Secondary Outcome Measure:

Measure Title	PFS From the Start of First-Line Therapy
Measure Description	PFS from the start of first-line therapy was defined as the interval between the start of first-line therapy and the date at which second disease progression (after the start of beyond progression therapy) was documented. Progression of disease was evaluated using RECIST version 1.1 and abdominal/pelvic CT or MRI scanning. The same method of assessment and the same technique were to be used to evaluate each lesion throughout the entire study. If more than one method was used, data from the most accurate method according to RECIST were recorded. Median PFS was estimated using the Kaplan-Meier method.
Time Frame	Baseline, every 9 weeks until disease progression, at end of treatment or withdrawal, for up to 24 months
Safety Issue?	No

Analysis Population Description
ITT population.

Reporting Groups

	Description
Bevacizumab + Oxaliplatin + Capecitabine	Participants received bevacizumab 7.5 mg/kg IV on Day 1; oxaliplatin 130 mg/m^2 IV on Day 1; and capecitabine 1000 mg/m^2, PO, BID on Days 1 through 14 (followed by 1-week rest period). The cycle was repeated every 3 weeks until disease progression.
Bevacizumab + FOLFOX	Participants received bevacizumab 5.0 mg/kg IV on Day 1 and FOLFOX (5-FU plus leucovorin and oxaliplatin) administered on Days 1 and 2 (followed by a rest period on Days 3 through 14); the specific FOLFOX regimen was determined on an individual participant basis by the investigator (5-FU and leucovorin dose was dependent on choice of FOLFOX regimen; oxaliplatin was administered at a dose ranging from 85 to 130 mg/m^2 IV on Day 1 based on choice of FOLFOX regimen). The cycle was repeated every 2 weeks until disease progression.

Measured Values

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
Number of Participants Analyzed	25	50
PFS From the Start of First-Line Therapy [units: months] Median (95% Confidence Interval)	17.8 (14.1 to 19.4)	18.0 (15.0 to 19.9)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants With an Overall Response of Complete Response (CR) or Partial Response (PR)
Measure Description	Percentage of participants with an overall response of CR or PR according to RECIST criteria. 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]). 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	Baseline, every 9 weeks until disease progression, at end of treatment or withdrawal, for up to 24 months
Safety Issue?	No

Analysis Population Description

ITT population; only participants with RECIST evaluations were included in the analysis.

Reporting Groups

	Description
Bevacizumab + Oxaliplatin + Capecitabine	Participants received bevacizumab 7.5 mg/kg IV on Day 1; oxaliplatin 130 mg/m^2 IV on Day 1; and capecitabine 1000 mg/m^2, PO, BID on Days 1 through 14 (followed by 1-week rest period). The cycle was repeated every 3 weeks until disease progression.
Bevacizumab + FOLFOX	Participants received bevacizumab 5.0 mg/kg IV on Day 1 and FOLFOX (5-FU plus leucovorin and oxaliplatin) administered on Days 1 and 2 (followed by a rest period on Days 3 through 14); the specific FOLFOX regimen was determined on an individual participant basis by the investigator (5-FU and leucovorin dose was dependent on choice of FOLFOX regimen; oxaliplatin was administered at a dose ranging from 85 to 130 mg/m^2 IV on Day 1 based on choice of FOLFOX regimen). The cycle was repeated every 2 weeks until disease progression.

Measured Values

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
Number of Participants Analyzed	22	47
Percentage of Participants With an Overall Response of Complete Response (CR) or Partial Response (PR) [units: percentage of participants]	27.3	6.4

4. Secondary Outcome Measure:

Measure Title	Geometric Mean Values of Pro-Angiogenic Cytokine Concentrations at Baseline and Prior to Progression
Measure Description	Pro-angiogenic cytokine concentrations of placental growth factor (PlGF), basic fibroblast growth factor (bFGF), and hepatocyte growth factor (HGF) in participant sera were measured and reported in units of picograms/milliliter (pg/mL). The geometric mean was calculated as exp10 (mean of log10 transformed concentration) and the standard deviation (SD) is SD of log10 transformed concentration.
Time Frame	Baseline, every 9 weeks until disease progression, at final visit or at withdrawal, for up to 24 months
Safety Issue?	No

Analysis Population Description

ITT Population. Number (n) equals (=) number of participants assessed for the given parameter at the specified visit.

Reporting Groups

	Description
Bevacizumab + Oxaliplatin + Capecitabine	Participants received bevacizumab 7.5 mg/kg IV on Day 1; oxaliplatin 130 mg/m^2 IV on Day 1; and capecitabine 1000 mg/m^2, PO, BID on Days 1 through 14 (followed by 1-week rest period). The cycle was repeated every 3 weeks until disease progression.

	Description
Bevacizumab + FOLFOX	Participants received bevacizumab 5.0 mg/kg IV on Day 1 and FOLFOX (5-FU plus leucovorin and oxaliplatin) administered on Days 1 and 2 (followed by a rest period on Days 3 through 14); the specific FOLFOX regimen was determined on an individual participant basis by the investigator (5-FU and leucovorin dose was dependent on choice of FOLFOX regimen; oxaliplatin was administered at a dose ranging from 85 to 130 mg/m^2 IV on Day 1 based on choice of FOLFOX regimen). The cycle was repeated every 2 weeks until disease progression.

Measured Values

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
Number of Participants Analyzed	13	23
Geometric Mean Values of Pro-Angiogenic Cytokine Concentrations at Baseline and Prior to Progression [units: pg/mL] Geometric Mean (Standard Deviation)		
Baseline bFGF (n=13,23)	6.8 (0.7)	6.1 (0.6)
bFGF, Prior to progression levels (n=12,18)	3.6 (0.9)	4.2 (0.7)
Baseline HGF (n=13,23)	133.0 (0.3)	186.0 (0.4)
HGF, Prior to progression levels (n=12,18)	187.3 (0.4)	230.3 (0.4)
Baseline PIGF (n=13,23)	29.8 (0.1)	26.3 (0.2)
PIGF, Prior to progression levels (n=12,18)	34.7 (0.1)	37.1 (0.2)

Reported Adverse Events

Time Frame	Adverse events (AEs) were reported from Day 1 until 28 days after last dose of study medication for up to 24 months.
Additional Description	The safety population included all participants who received at least 1 dose of the investigational or non-investigational products.

Reporting Groups

	Description
Bevacizumab + Oxaliplatin + Capecitabine	Participants received bevacizumab 7.5 mg/kg IV on Day 1; oxaliplatin 130 mg/m^2 IV on Day 1; and capecitabine 1000 mg/m^2, PO, BID on Days 1 through 14 (followed by 1-week rest period). The cycle was repeated every 3 weeks until disease progression.
Bevacizumab + FOLFOX	Participants received bevacizumab 5.0 mg/kg IV on Day 1 and FOLFOX (5-FU plus leucovorin and oxaliplatin) administered on Days 1 and 2 (followed by a rest period on Days 3 through 14); the specific FOLFOX regimen was determined on an individual participant basis by the investigator (5-FU and leucovorin dose was dependent on choice of FOLFOX regimen; oxaliplatin was administered at a dose ranging from 85 to 130 mg/m^2 IV on Day 1 based on choice of FOLFOX regimen). The cycle was repeated every 2 weeks until disease progression.

Serious Adverse Events

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
	Affected/At Risk (%)	Affected/At Risk (%)
Total	12/25 (48%)	18/50 (36%)
Blood and lymphatic system disorders		
Febrile neutropenia [A] *	0/25 (0%)	1/50 (2%)
Gastrointestinal disorders		
Abdominal pain [A] *	1/25 (4%)	1/50 (2%)
Abdominal pain upper [A] *	1/25 (4%)	1/50 (2%)
Anal fistula [A] *	1/25 (4%)	0/50 (0%)
Colonic obstruction [A] *	0/25 (0%)	1/50 (2%)
Diarrhoea [A] *	1/25 (4%)	2/50 (4%)
Enteritis [A] *	1/25 (4%)	0/50 (0%)
Ileus [A] *	0/25 (0%)	1/50 (2%)
Intestinal perforation [A] *	0/25 (0%)	1/50 (2%)
Nausea [A] *	0/25 (0%)	1/50 (2%)
Vomiting [A] *	1/25 (4%)	1/50 (2%)
General disorders		

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
	Affected/At Risk (%)	Affected/At Risk (%)
Asthenia [A] *	1/25 (4%)	0/50 (0%)
Device dislocation [A] *	0/25 (0%)	1/50 (2%)
Disease progression [A] *	0/25 (0%)	1/50 (2%)
Drug intolerance [A] *	0/25 (0%)	1/50 (2%)
General physical health deterioration [A] *	0/25 (0%)	3/50 (6%)
Idiosyncratic drug reaction [A] *	0/25 (0%)	1/50 (2%)
Obstruction [A] *	1/25 (4%)	0/50 (0%)
Pain [A] *	0/25 (0%)	1/50 (2%)
Infections and infestations		
Necrotising fasciitis [A] *	0/25 (0%)	1/50 (2%)
Perirectal abscess [A] *	0/25 (0%)	1/50 (2%)
Sepsis [A] *	0/25 (0%)	1/50 (2%)
Vaginal abscess [A] *	1/25 (4%)	0/50 (0%)
Injury, poisoning and procedural complications		
Drug toxicity [A] *	2/25 (8%)	0/50 (0%)
Fall [A] *	1/25 (4%)	0/50 (0%)
Jaw fracture [A] *	1/25 (4%)	0/50 (0%)
Metabolism and nutrition disorders		
Decreased appetite [A] *	1/25 (4%)	1/50 (2%)
Dehydration [A] *	2/25 (8%)	1/50 (2%)
Nervous system disorders		
Epilepsy [A] *	1/25 (4%)	0/50 (0%)
Psychiatric disorders		

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
	Affected/At Risk (%)	Affected/At Risk (%)
Confusional state [A] *	1/25 (4%)	0/50 (0%)
Depression [A] *	1/25 (4%)	0/50 (0%)
Respiratory, thoracic and mediastinal disorders		
Dyspnoea [A] *	0/25 (0%)	1/50 (2%)
Hiccups [A] *	1/25 (4%)	0/50 (0%)
Skin and subcutaneous tissue disorders		
Urticaria [A] *	0/25 (0%)	1/50 (2%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.0)

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

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
	Affected/At Risk (%)	Affected/At Risk (%)
Total	24/25 (96%)	49/50 (98%)
Blood and lymphatic system disorders		
Anaemia [A] *	1/25 (4%)	8/50 (16%)
Leukopenia [A] *	1/25 (4%)	4/50 (8%)
Lymphopenia [A] *	0/25 (0%)	1/50 (2%)
Neutropenia [A] *	4/25 (16%)	10/50 (20%)
Thrombocytopenia [A] *	4/25 (16%)	7/50 (14%)
Cardiac disorders		
Angina pectoris [A] *	1/25 (4%)	0/50 (0%)
Arrhythmia [A] *	0/25 (0%)	1/50 (2%)
Arteriospasm coronary [A] *	0/25 (0%)	1/50 (2%)

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
	Affected/At Risk (%)	Affected/At Risk (%)
Atrial fibrillation [A] *	1/25 (4%)	0/50 (0%)
Palpitation [A] *	0/25 (0%)	1/50 (2%)
Pericardial effusion [A] *	0/25 (0%)	1/50 (2%)
Tachycardia [A] *	0/25 (0%)	1/50 (2%)
Eye disorders		
Lacrimation increased [A] *	1/25 (4%)	1/50 (2%)
Gastrointestinal disorders		
Abdominal distension [A] *	1/25 (4%)	0/50 (0%)
Abdominal pain [A] *	9/25 (36%)	13/50 (26%)
Abdominal pain lower [A] *	1/25 (4%)	0/50 (0%)
Abdominal pain upper [A] *	2/25 (8%)	3/50 (6%)
Anal fistula [A] *	0/25 (0%)	1/50 (2%)
Anal haemorrhage [A] *	1/25 (4%)	1/50 (2%)
Aphthous stomatitis [A] *	0/25 (0%)	1/50 (2%)
Ascites [A] *	1/25 (4%)	1/50 (2%)
Colitis [A] *	2/25 (8%)	0/50 (0%)
Constipation [A] *	4/25 (16%)	6/50 (12%)
Diarrhoea [A] *	14/25 (56%)	21/50 (42%)
Duodenitis [A] *	0/25 (0%)	1/50 (2%)
Dyspepsia [A] *	0/25 (0%)	7/50 (14%)
Dysphagia [A] *	1/25 (4%)	1/50 (2%)
Epigastric discomfort [A] *	0/25 (0%)	1/50 (2%)

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
	Affected/At Risk (%)	Affected/At Risk (%)
Faecaloma [A] *	0/25 (0%)	1/50 (2%)
Frequent bowel movements [A] *	0/25 (0%)	1/50 (2%)
Gastrointestinal motility disorder [A] *	1/25 (4%)	0/50 (0%)
Gastrooesophageal reflux disease [A] *	0/25 (0%)	1/50 (2%)
Haemorrhoids [A] *	0/25 (0%)	1/50 (2%)
Intestinal obstruction [A] *	1/25 (4%)	0/50 (0%)
Nausea [A] *	10/25 (40%)	16/50 (32%)
Oesophagitis [A] *	1/25 (4%)	0/50 (0%)
Oral disorder [A] *	0/25 (0%)	1/50 (2%)
Proctalgia [A] *	0/25 (0%)	2/50 (4%)
Rectal tenesmus [A] *	0/25 (0%)	2/50 (4%)
Small intestinal obstruction [A] *	0/25 (0%)	1/50 (2%)
Steatorrhoea [A] *	1/25 (4%)	0/50 (0%)
Stomatitis [A] *	2/25 (8%)	4/50 (8%)
Vomiting [A] *	6/25 (24%)	5/50 (10%)
General disorders		
Asthenia [A] *	5/25 (20%)	7/50 (14%)
Chest pain [A] *	1/25 (4%)	1/50 (2%)
Chills [A] *	1/25 (4%)	1/50 (2%)
Fatigue [A] *	9/25 (36%)	22/50 (44%)
Feeling cold [A] *	1/25 (4%)	0/50 (0%)
General physical health deterioration [A] *	3/25 (12%)	0/50 (0%)

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
	Affected/At Risk (%)	Affected/At Risk (%)
Mucosal inflammation [A] *	1/25 (4%)	2/50 (4%)
Oedema [A] *	1/25 (4%)	0/50 (0%)
Oedema peripheral [A] *	1/25 (4%)	1/50 (2%)
Pain [A] *	2/25 (8%)	4/50 (8%)
Pyrexia [A] *	3/25 (12%)	8/50 (16%)
Systemic inflammatory response syndrome [A] *	0/25 (0%)	1/50 (2%)
Hepatobiliary disorders		
Hepatic pain [A] *	0/25 (0%)	2/50 (4%)
Hepatomegaly [A] *	0/25 (0%)	1/50 (2%)
Liver disorder [A] *	0/25 (0%)	1/50 (2%)
Immune system disorders		
Drug hypersensitivity [A] *	2/25 (8%)	5/50 (10%)
Hypersensitivity [A] *	0/25 (0%)	1/50 (2%)
Infections and infestations		
Anal abscess [A] *	0/25 (0%)	1/50 (2%)
Bronchitis [A] *	0/25 (0%)	1/50 (2%)
Escherichia infection [A] *	0/25 (0%)	1/50 (2%)
Eye infection [A] *	1/25 (4%)	1/50 (2%)
Febrile infection [A] *	0/25 (0%)	1/50 (2%)
Gastroenteritis [A] *	0/25 (0%)	1/50 (2%)
Infection [A] *	1/25 (4%)	0/50 (0%)
Lung infection [A] *	1/25 (4%)	0/50 (0%)

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
	Affected/At Risk (%)	Affected/At Risk (%)
Nail infection [A] *	0/25 (0%)	1/50 (2%)
Nasopharyngitis [A] *	0/25 (0%)	3/50 (6%)
Paronychia [A] *	1/25 (4%)	0/50 (0%)
Pharyngitis [A] *	0/25 (0%)	1/50 (2%)
Respiratory tract infection [A] *	0/25 (0%)	1/50 (2%)
Rhinitis [A] *	1/25 (4%)	0/50 (0%)
Sinusitis [A] *	0/25 (0%)	1/50 (2%)
Tooth abscess [A] *	0/25 (0%)	2/50 (4%)
Tooth infection [A] *	1/25 (4%)	1/50 (2%)
Tracheitis [A] *	1/25 (4%)	0/50 (0%)
Upper respiratory tract infection [A] *	1/25 (4%)	0/50 (0%)
Urinary tract infection [A] *	0/25 (0%)	2/50 (4%)
Injury, poisoning and procedural complications		
Contusion [A] *	1/25 (4%)	0/50 (0%)
Investigations		
Blood alkaline phosphatase increased [A] *	0/25 (0%)	1/50 (2%)
Blood creatinine [A] *	0/25 (0%)	1/50 (2%)
Blood creatinine increased [A] *	0/25 (0%)	1/50 (2%)
Body temperature increased [A] *	0/25 (0%)	1/50 (2%)
Gamma-glutamyltransferase abnormal [A] *	0/25 (0%)	1/50 (2%)
Gamma-glutamyltransferase increased [A] *	0/25 (0%)	3/50 (6%)
Weight decreased [A] *	3/25 (12%)	2/50 (4%)

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
	Affected/At Risk (%)	Affected/At Risk (%)
White blood cell count decreased [A] *	0/25 (0%)	1/50 (2%)
Metabolism and nutrition disorders		
Decreased appetite [A] *	9/25 (36%)	12/50 (24%)
Dehydration [A] *	1/25 (4%)	1/50 (2%)
Gout [A] *	1/25 (4%)	0/50 (0%)
Hyperglycaemia [A] *	1/25 (4%)	2/50 (4%)
Hypoalbuminaemia [A] *	0/25 (0%)	4/50 (8%)
Hypocalcaemia [A] *	0/25 (0%)	3/50 (6%)
Hypokalaemia [A] *	0/25 (0%)	4/50 (8%)
Hypomagnesaemia [A] *	0/25 (0%)	1/50 (2%)
Hyponatraemia [A] *	0/25 (0%)	2/50 (4%)
Hypophosphataemia [A] *	0/25 (0%)	1/50 (2%)
Vitamin D deficiency [A] *	1/25 (4%)	1/50 (2%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] *	1/25 (4%)	2/50 (4%)
Back pain [A] *	3/25 (12%)	6/50 (12%)
Flank pain [A] *	0/25 (0%)	1/50 (2%)
Muscle contracture [A] *	1/25 (4%)	0/50 (0%)
Muscle spasms [A] *	0/25 (0%)	2/50 (4%)
Muscular weakness [A] *	1/25 (4%)	0/50 (0%)
Musculoskeletal chest pain [A] *	0/25 (0%)	1/50 (2%)
Musculoskeletal pain [A] *	1/25 (4%)	1/50 (2%)

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
	Affected/At Risk (%)	Affected/At Risk (%)
Myalgia [A] *	1/25 (4%)	0/50 (0%)
Osteoarthritis [A] *	0/25 (0%)	1/50 (2%)
Pain in extremity [A] *	0/25 (0%)	3/50 (6%)
Sensation of heaviness [A] *	0/25 (0%)	1/50 (2%)
Spinal osteoarthritis [A] *	0/25 (0%)	1/50 (2%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Metastatic pain [A] *	0/25 (0%)	1/50 (2%)
Nervous system disorders		
Coordination abnormal [A] *	0/25 (0%)	1/50 (2%)
Dysaesthesia [A] *	3/25 (12%)	1/50 (2%)
Dysgeusia [A] *	2/25 (8%)	2/50 (4%)
Memory impairment [A] *	1/25 (4%)	0/50 (0%)
Neuropathy peripheral [A] *	7/25 (28%)	9/50 (18%)
Neurotoxicity [A] *	0/25 (0%)	3/50 (6%)
Paraesthesia [A] *	6/25 (24%)	10/50 (20%)
Peripheral sensory neuropathy [A] *	5/25 (20%)	0/50 (0%)
Polyneuropathy [A] *	3/25 (12%)	7/50 (14%)
Restless legs syndrome [A] *	1/25 (4%)	0/50 (0%)
Sensory disturbance [A] *	0/25 (0%)	2/50 (4%)
Tremor [A] *	0/25 (0%)	1/50 (2%)
Psychiatric disorders		
Anxiety [A] *	1/25 (4%)	1/50 (2%)

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
	Affected/At Risk (%)	Affected/At Risk (%)
Apathy [A] *	0/25 (0%)	2/50 (4%)
Disorientation [A] *	0/25 (0%)	1/50 (2%)
Insomnia [A] *	2/25 (8%)	3/50 (6%)
Renal and urinary disorders		
Haematuria [A] *	1/25 (4%)	0/50 (0%)
Proteinuria [A] *	1/25 (4%)	2/50 (4%)
Renal pain [A] *	0/25 (0%)	1/50 (2%)
Reproductive system and breast disorders		
Breast cyst [A] *	0/25 (0%)	1/50 (2%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] *	3/25 (12%)	2/50 (4%)
Dysphonia [A] *	0/25 (0%)	1/50 (2%)
Dyspnoea [A] *	2/25 (8%)	3/50 (6%)
Dyspnoea exertional [A] *	0/25 (0%)	1/50 (2%)
Epistaxis [A] *	2/25 (8%)	4/50 (8%)
Increased upper airway secretion [A] *	0/25 (0%)	1/50 (2%)
Oropharyngeal pain [A] *	1/25 (4%)	1/50 (2%)
Productive cough [A] *	1/25 (4%)	0/50 (0%)
Rhinorrhoea [A] *	2/25 (8%)	1/50 (2%)
Rhonchi [A] *	1/25 (4%)	0/50 (0%)
Throat irritation [A] *	0/25 (0%)	1/50 (2%)
Skin and subcutaneous tissue disorders		
Acne [A] *	0/25 (0%)	1/50 (2%)

	Bevacizumab + Oxaliplatin + Capecitabine	Bevacizumab + FOLFOX
	Affected/At Risk (%)	Affected/At Risk (%)
Alopecia [A] *	1/25 (4%)	1/50 (2%)
Angioedema [A] *	1/25 (4%)	0/50 (0%)
Dermatitis allergic [A] *	1/25 (4%)	0/50 (0%)
Hyperhidrosis [A] *	0/25 (0%)	1/50 (2%)
Night sweats [A] *	0/25 (0%)	1/50 (2%)
Palmar-plantar erythrodysaesthesia syndrome [A] *	8/25 (32%)	2/50 (4%)
Petechiae [A] *	0/25 (0%)	1/50 (2%)
Rash [A] *	1/25 (4%)	2/50 (4%)
Skin chapped [A] *	1/25 (4%)	0/50 (0%)
Vascular disorders		
Deep vein thrombosis [A] *	0/25 (0%)	1/50 (2%)
Hypertension [A] *	3/25 (12%)	13/50 (26%)
Vascular insufficiency [A] *	0/25 (0%)	1/50 (2%)

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (13.0)

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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