ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 07/21/2015

ClinicalTrials.gov ID: NCT00577031

Study Identification

Unique Protocol ID:	ML21380
Brief Title:	OBELIX Study: A Study of Avastin (Bevacizumab) in Combination With XELOX in Patients With Metastatic Cancer of the Colon or Rectum.
Official Title:	Open-label, Efficacy and Safety Study of Bevacizumab (Avastin®) in Combination With XELOX (Oxaliplatin Plus Xeloda®) for the First-line Treatment of Patients With Metastatic Cancer of the Colon or Rectum - 'OBELIX'
Secondary IDs:	

Study Status

Record Verification:	July 2015
Overall Status:	Completed
Study Start:	February 2008
Primary Completion:	August 2011 [Actual]
Study Completion:	August 2011 [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: Rubrica N. 33/SP Board Name: Comitato Etico per la Sperimentazione Clinica dei Medicinali dell' Azienda Ospedaliero Board Affiliation: Universitaria Careggi Phone: +39 055 7947396 Email: cesf01@aou-careggi.toscana.it
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	Italy: Ministry of Health

Study Description

Brief Summary:	This single arm study will evaluate the efficacy and safety of a first-line regimen of Avastin and XELOX (oxaliplatin + Xeloda) in patients with metastatic cancer of the colon or rectum. Patients will receive 21-day cycles of treatment, comprising Avastin 7.5mg/kg iv on day 1, oxaliplatin 130mg/m2 iv on day 1, and Xeloda 1000mg/m2 po twice daily on days 1-14, for a maximum of 6 months. Patients with stable disease or complete or partial response may continue on Avastin therapy. The anticipated time on study treatment is until disease progression, and the target sample size is 100-500 individuals.
Detailed Description:	

Conditions

Conditions:	Colorectal Cancer
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 4
Intervention Model:	Single Group Assignment
Number of Arms:	1
Masking:	Open Label
Allocation:	N/A
Endpoint Classification:	Safety/Efficacy Study

Enrollment: 205 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: 1	Drug: bevacizumab [Avastin] 7.5mg iv on day 1 of each 3 week cycle Drug: Oxaliplatin 130mg/m2 iv on day 1 of each 3 week cycle Drug: Xeloda 1000mg/m2 po bid on days 1-14 of each 3 week cycle

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;
- locally advanced or metastatic colorectal cancer;
- no previous treatment with chemotherapy for metastatic disease;
- at least one measurable lesion.

Exclusion Criteria:

- radiotherapy to any site within 4 weeks before study;
- untreated brain metastases or primary brain tumors;
- clinically significant cardiovascular disease;
- chronic daily treatment with high dose aspirin (>325 mg/day);
- other co-existing malignancies or malignancies diagnosed within last 5 years.

Contacts/Locations

Study Officials: Clinical Trials
Study Director

Hoffmann-La Roche

Locations: Italy

Fano, Italy, 61032

Catanzaro, Italy, 88100

Roma, Italy, 00152

Orbassano, Italy, 10043

Firenze, Italy, 50139

Roma, Italy, 00189

Padova, Italy, 35128

Pavia, Italy, 27100

Caserta, Italy, 81100

Roma, Italy, 00184

Salerno, Italy, 84131

Torino, Italy, 10153

Ivrea, Italy, 10015

Bologna, Italy, 40138

Reggio Emilia, Italy, 42100

Rionero in Vulture, Italy, 85028

Lecce, Italy, 73100

Legnano, Italy, 20025

Palermo, Italy, 90146

Negrar, Italy, 37024

Latisana, Italy, 33053

Palermo, Italy, 90127

Sondrio, Italy, 23100

Cagliari, Italy, 09121

Cefalu, Italy, 90015

Frattaminore, Italy, 80026

Taormina, Italy, 98030

Cagliari, Italy, 09100

Legnago, Italy, 37045

Napoli, Italy, 80131

Reggio Calabria, Italy, 89100

Verbania, Italy, 28921

Brescia, Italy, 25122

San Giovanni Rotondo, Italy, 71013

Grosseto, Italy, 58100

Roma, Italy, 00186

Macerata, Italy, 62100

Torino, Italy, 10125

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Reporting Groups

	Description
Bevacizumab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression, participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Overall Study

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
Started	205
Completed	0
Not Completed	205
Adverse Event	52
Progression of disease	93
Protocol Violation	5
Participant withdrew consent	13
Participant non-compliance	5
Need for surgery	17
Medical decision	14
Death	6

Baseline Characteristics

Analysis Population Description

Safety population: all enrolled participants who received at least 1 dose of all study medications.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Baseline Measures

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants	197
Age, Continuous [units: years] Mean (Standard Deviation)	62.25 (9.94)
Gender, Male/Female [units: participants]	
Female	86
Male	111

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Progression-Free Survival (PFS): Percentage of Participants With Progressive Disease or Death
Measure Description	PFS was defined as the time period in months from the start of study treatment to the first observation of disease progression or death from any cause, whichever occurred first. Data for participants with no tumor assessments after baseline but who were still alive at the time of the clinical cutoff were censored at Day 1. Participants who underwent surgery after experiencing a sufficient shrinkage of the tumor, had any relapse, new occurrence of colorectal cancer, or who died were all considered as having had an event. Participants who underwent surgery without any such event were censored at the date of the last tumor assessment that documented neither a relapse nor a new colorectal cancer had occurred. Progression is defined using Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.0), as a 20 percent (%) 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.
Time Frame	Baseline and Day 1 of every cycle until disease progression or death up to 5 years
Safety Issue?	No

Analysis Population Description

Intent-to-treat (ITT) population: all enrolled participants who received at least 1 dose of all study medications and had at least 1 measurable lesion according to the Response Evaluation Criteria In Solid Tumours (RECIST) criteria.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (3-week cycles): Participants received bevacizumab 7.5 mg/kg IV) and oxaliplatin 130 mg mg/m^2 IV on Day 1 and capecitabine 1000 mg/m^2 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	197
Progression-Free Survival (PFS): Percentage of Participants With Progressive Disease or Death [units: percentage of participants]	50.25

2. Primary Outcome Measure:

Measure Title	PFS: Time to Event
Measure Description	PFS was defined as the time period in months from the start of study treatment to the first observation of disease progression or death from any cause, whichever occurred first. Data for participants with no tumor assessments after baseline but who were still alive at the time of the clinical cutoff were censored at Day 1. Participants who underwent surgery after experiencing a sufficient shrinkage of the tumor, had any relapse, new occurrence of colorectal cancer, or who died were all considered as having had an event. Participants who underwent surgery without any such event were censored at the date of the last tumor assessment that documented that neither a relapse nor a new colorectal cancer had occurred. Median PFS was estimated using the Kaplan-Meier method.
Time Frame	Baseline and Day 1 of every cycle until disease progression or death up to 5 years
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (3-week cycles): Participants received bevacizumab 7.5 mg/kg IV) and oxaliplatin 130 mg mg/m^2 IV on Day 1 and capecitabine 1000 mg/m^2 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	197
PFS: Time to Event [units: months] Median (95% Confidence Interval)	9.70 (8.43 to 10.49)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Best Overall Response of Complete Response (CR) or Partial Response (PR) Among Participants in the ITT Population Who Had at Least 1 Post-Baseline Assessment
Measure Description	The percentage of participants with a best overall response of CR or PR according to 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]). No new lesions. PR was defined as a greater than or equal to (≥) 30% 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 (every 3 cycles) until end of treatment, disease progression, or withdrawal up to 5 years
Safety Issue?	No

Analysis Population Description

Subset of participants in the ITT population who had at least 1 post-baseline tumor assessment.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	165
Percentage of Participants With a Best Overall Response of Complete Response (CR) or Partial Response (PR) Among Participants in the ITT Population Who Had at Least 1 Post-Baseline Assessment [units: percentage of participants]	58.79

4. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a CR or PR Among Participants in the ITT Population
Measure Description	CR and PR were defined using RECIST v1.0. 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 <10 mm). No new lesions. PR was defined as a ≥30% 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 (every 3 cycles) until end of treatment, disease progression, or withdrawal up to 5 years
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	197
Percentage of Participants With a CR or PR Among Participants in the ITT Population [units: percentage of participants]	49.24

5. Secondary Outcome Measure:

Measure Title	Time to CR or PR Overall Response - Time to Event
Measure Description	Time to overall response (CR or PR) was calculated as the time between the date of start of treatment until first documented response (CR or PR defined per RECIST v1.0). Participants who did not achieve CR or PR were censored at the date of progression, death, or at last adequate tumor assessment date. Median time to CR or PR overall response was estimated using the Kaplan-Meier method.
Time Frame	Baseline, every 9 weeks (every 3 cycles) until end of treatment, disease progression, or withdrawal up to 5 years
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	197
Time to CR or PR Overall Response - Time to Event [units: months] Median (95% Confidence Interval)	3.93 (2.56 to 4.66)

6. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Best Overall Response of CR or PR During First Line Treatment
Measure Description	CR and PR were defined using RECIST v1.0 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 <10 mm). No new lesions. PR was defined as a ≥30% decrease under baseline of the sum of diameters of all target lesions. Short axis was used in sum for target nodes, while longest diameter was used in sum for all other target lesions. No unequivocal progression of non-target disease. No new lesions.
Time Frame	Baseline, every 3 weeks (every cycle) to disease progression or death up to 5 years
Safety Issue?	No

Analysis Population Description

ITT population, only those participants who achieved a best overall response of CR or PR during first line treatment were included in the analysis.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles):If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	97
Percentage of Participants With a Best Overall Response of CR or PR During First Line Treatment [units: percentage of participants]	54.64

7. Secondary Outcome Measure:

Measure Title	Duration of Overall Response Among Participants Whose Best Response Was CR or PR During First Line Treatment - Time to Event
Measure Description	For participants with a best overall response of CR or PR, the duration of overall response was measured from the time that the criteria for CR or PR (whichever occurred first) was met until the first date that progressive disease was objectively documented or until the date of death due to underlying cancer, whichever occurred first. Data for participants who did not have an event or who were alive without an objectively documented progressive disease were censored at the date of last adequate tumor assessment. Median duration of overall response was estimated using the Kaplan-Meier method.
Time Frame	Baseline, every 3 weeks (every cycle) to disease progression or death up to 5 years
Safety Issue?	No

Analysis Population Description

ITT population, only those participants who achieved a best overall response of CR or PR during first line treatment were included in the analysis.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles):If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	97
Duration of Overall Response Among Participants Whose Best Response Was CR or PR During First Line Treatment - Time to Event [units: months] Median (95% Confidence Interval)	8.52 (7.28 to 10.33)

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Stable Response During First Line Treatment

Measure Description	Stable response defined as participants with a best overall response of CR, PR, or stable disease (SD), defined using RECIST v1.0 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 <10 mm). No new lesions. PR was defined as a ≥30% 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. SD defined as neither sufficient shrinkage to qualify for partial response nor sufficient increase to qualify for progressive disease, taking as reference the smallest sum longest diameter since the treatment started.
Time Frame	Baseline, every 3 weeks (every cycle) to disease progression or death up to 5 years
Safety Issue?	No

Analysis Population Description

ITT population, only participants who achieved a best overall response of CR, PR, or SD during first line treatment were included in the analysis.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	152
Percentage of Participants With a Stable Response During First Line Treatment [units: percentage of participants]	52.63

9. Secondary Outcome Measure:

Measure Title	Duration of Stable Response

Measure Description	For participants with a best overall response of CR, PR, or SD during first line treatment, the duration of stable response was measured from the time that the criteria for CR, PR, or SD (whichever occurred first) was met until the first date that progressive disease was objectively documented or until the date of death due to underlying cancer, whichever occurred first. Data for participants who did not have an event or who were alive without an objectively documented progressive disease were censored at the date of last adequate tumor assessment. Median duration of stable response was estimated using the Kaplan-Meier method.
Time Frame	Baseline, every 3 weeks (every cycle) to disease progression or death up to 5 years
Safety Issue?	No

Analysis Population Description

ITT population, only participants who achieved a best overall response of CR, PR, or SD during first line treatment were included in the analysis.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	152
Duration of Stable Response [units: months] Median (95% Confidence Interval)	10.39 (9.02 to 11.44)

10. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Treatment Failure
Measure Description	Treatment-failure was defined as discontinuation of treatment for any reason, including the following qualifying events: death due to any cause, adverse event, insufficient therapeutic response (progression of disease), failure to return (lost to follow-up), refusing treatment (participant non-compliance), being unwilling to cooperate and withdrawing consent (participant withdrew consent).
Time Frame	Baseline, every 3 weeks (every cycle) to disease progression or death up to 5 years
Safety Issue?	No

Analysis Population Description
ITT population.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	197
Percentage of Participants With Treatment Failure [units: percentage of participants]	82.74

11. Secondary Outcome Measure:

Measure Title	Time to Treatment Failure
Measure Description	Time to treatment-failure was defined as the time from the first day of treatment to discontinuation of treatment for any reason, including: death due to any cause, adverse event, insufficient therapeutic response (progression of disease), failure to return (lost to follow-up), refusing treatment (participant non-compliance), being unwilling to cooperate and withdrawing consent (participant withdrew consent). For participants who did not experience a qualifying event, their data were censored at the earlier of either the date of last tumour assessment or the date of the last intake of study medication. Median time to treatment-failure was estimated using the Kaplan-Meier method.
Time Frame	Baseline, every 3 weeks (every cycle) to disease progression or death up to 5 years
Safety Issue?	No

Analysis Population Description
ITT population.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	197
Time to Treatment Failure [units: months] Median (95% Confidence Interval)	6.69 (5.97 to 7.74)

12. Secondary Outcome Measure:

Measure Title	Overall Survival: Percentage of Participants That Died Due to Any Cause
Measure Description	Overall survival was defined as the time from the date of the first day of treatment until the date of death from any cause. If a participant was not known to have died, survival was censored at the last date the participant was known to be alive.
Time Frame	Baseline, Day 1 of every cycle to end-of-treatment, every 3 months during longer-term follow-up, or to death due to any cause up to 5 years
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	197
Overall Survival: Percentage of Participants That Died Due to Any Cause [units: percentage of participants]	50.76

13. Secondary Outcome Measure:

Measure Title	Overall Survival: Time to Event
Measure Description	Overall survival was defined as the time from the date of the first day of treatment until the date of death from any cause. If a participant was not known to have died, survival was censored at the last date the participant was known to be alive. Median overall survival was estimated using the Kaplan-Meier method.
Time Frame	Baseline, Day 1 of every cycle to end-of-treatment, every 3 months during longer-term follow-up, or to death due to any cause up to 5 years
Safety Issue?	No

Analysis Population Description

ITT population.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	197
Overall Survival: Time to Event [units: months] Median (95% Confidence Interval)	23.15 (20.07 to 27.15)

14. Secondary Outcome Measure:

Measure Title	Percentage of Participants Undergoing Surgical Intervention With Residual Disease Status Post-surgery
Measure Description	The percentage of participants who underwent surgery during the study period with an evaluation of their disease status after surgery. The surgery during the study period was described by reason: curative, palliative, biopsy, other, or unknown. Residual disease status after surgery was described as: no residual disease due to radical surgery, presence of residual disease, unknown or not applicable.
Time Frame	At surgery, at least 6 to 8 weeks after last dose of bevacizumab up to 5 years
Safety Issue?	No

Analysis Population Description

The 52 participant subpopulation of the ITT population who underwent surgery during the time period of the study.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	52
Percentage of Participants Undergoing Surgical Intervention With Residual Disease Status Post-surgery [units: percentage of participants]	
Curative, no residual disease	55.77
Curative, residual disease	13.46
Curative, unknown	3.85
Curative, not applicable	7.69
Palliative, no residual disease	3.85
Palliative, residual disease	7.69
Palliative, unknown	3.85

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Palliative, not applicable	1.92
Biopsy, residual disease	1.92
Biopsy, not applicable	1.92
Unknown, unknown	1.92
Unknown, not applicable	3.85
Other, residual disease	1.92
Other, not applicable	3.85

15. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Best Overall Response of CR or PR by Kirsten Rat Sarcoma Viral Oncogene Homolog (K-Ras)/V-Raf Murine Sarcoma Viral Oncogene Homolog B (B-Raf) Mutation Status
Measure Description	The percentage of participants with a best overall response of CR or PR according to 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 <10 mm). No new lesions. PR was defined as ≥30% 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. The K-Ras and/or the B-Raf gene mutation status of participants was evaluated by the central laboratory using tumor samples. Wild-type participants did not have a mutation in either gene.
Time Frame	Baseline, every 9 weeks (every 3 cycles) until end of treatment, disease progression, or withdrawal up to 5 years
Safety Issue?	No

Analysis Population Description

ITT population; only participants with a known K-Ras and/or B-Raf gene mutation status and at least 1 post-baseline tumor assessment. Number (n) equals (=) number of participants with either wild-type or K-Ras/B-Raf gene mutation.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	33
Percentage of Participants With Best Overall Response of CR or PR by Kirsten Rat Sarcoma Viral Oncogene Homolog (K-Ras)/V-Raf Murine Sarcoma Viral Oncogene Homolog B (B-Raf) Mutation Status [units: percentage of participants]	
Wild-type (n=18)	88.89
Gene mutation (n=15)	66.67

16. Secondary Outcome Measure:

Measure Title	European Quality of Life 5 Dimension (EQ-5D) Raw-Index Score
Measure Description	Quality of life (QoL) assessments were used to derive pre-specified QoL scores according to the QoL manual “EQ-5D-3 Level (3L)" user guide for instrument version 4.0. The EQ-5D is a participant rated questionnaire to assess health-related quality of life in terms of a single index value. The visual analog scale (VAS) component rates current health state on a scale from 0 (worst imaginable health state) to 100 (best imaginable health state); higher scores indicate a better health state. The overall health score absolute changes were calculated for each participant as follows: (score at the end of treatment minus score at baseline). EQ-5D health states were converted into EQ-5D-3L raw index value by applying the scoring algorithm based on the European EQ-net VAS set. The raw index was chosen instead of rescaled index, since the questionnaire was used in order to obtain a quality of life assessment. The raw index scores ranged from 0 (worst health state) to 100 (best health state).
Time Frame	Baseline, every 9 weeks (every 3 cycles), at end-of-treatment up to 5 years
Safety Issue?	No

Analysis Population Description

ITT population, only participants who had EQ-5D-3L scores for both baseline and last visit were included in the analysis.

Reporting Groups

	Description
Bevucizamab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (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 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Measured Values

	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
Number of Participants Analyzed	114
European Quality of Life 5 Dimension (EQ-5D) Raw-Index Score [units: units on a scale] Mean (Standard Deviation)	
Baseline	80.24 (14.32)
Last visit	74.94 (19.08)
Absolute change from baseline	-5.30 (19.13)

Statistical Analysis 1 for European Quality of Life 5 Dimension (EQ-5D) Raw-Index Score

Statistical Analysis Overview	Comparison Groups	Bevucizamab+Oxaliplatin+Capecitabine/Bevacizumab
	Comments	Change from baseline to last visit
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0076
	Comments	[Not specified]
	Method	Other [Signed-rank test]
	Comments	[Not specified]

Reported Adverse Events

Time Frame	Adverse events (AE) were collected from the date of first administration of study treatment until 28 days after the last dose of study treatment up to 5 years
Additional Description	[Not specified]

Reporting Groups

	Description
Bevacizumab+Oxaliplatin +Capecitabine/Bevacizumab	Cycles 1-8 (3-week cycles): Participants received bevacizumab 7.5 mg/kg IV) and oxaliplatin 130 mg mg/m^2 IV on Day 1 and capecitabine 1000 mg/m^2 tablets, orally, every 12 hours starting the evening of Day 1 for 14 days continuously; cycle was repeated until disease progression or for a maximum of 8 cycles. Cycle 9 and beyond (3-week cycles): If the first 8 cycles were tolerated with no disease progression, participants received bevacizumab 7.5 mg/kg IV on Day 1; the cycle was repeated until disease progression.

Serious Adverse Events

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Total	56/197 (28.43%)
Blood and lymphatic system disorders	
Anaemia [A] *	1/197 (0.51%)
Cardiac disorders	
Cardiac arrest [A] *	1/197 (0.51%)
Cardio-respiratory arrest [A] *	1/197 (0.51%)
Cardiovascular disorder [A] *	1/197 (0.51%)
Coronary artery disease [A] *	1/197 (0.51%)
Myocardial infarction [A] *	1/197 (0.51%)
Gastrointestinal disorders	
Abdominal pain [A] *	1/197 (0.51%)
Abdominal strangulated hernia [A] *	1/197 (0.51%)
Anal fistula [A] *	1/197 (0.51%)

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Constipation [A] *	1/197 (0.51%)
Diarrhoea [A] *	4/197 (2.03%)
Gastrointestinal disorder [A] *	1/197 (0.51%)
Gastrointestinal inflammation [A] *	1/197 (0.51%)
Gastrointestinal obstruction [A] *	1/197 (0.51%)
Ileus paralytic [A] *	1/197 (0.51%)
Intestinal obstruction [A] *	2/197 (1.02%)
Intestinal perforation [A] *	2/197 (1.02%)
Nausea [A] *	1/197 (0.51%)
Peritonitis [A] *	1/197 (0.51%)
Subileus [A] *	4/197 (2.03%)
Vomiting [A] *	1/197 (0.51%)
General disorders	
Asthenia [A] *	2/197 (1.02%)
Chest pain [A] *	1/197 (0.51%)
Death [A] *	1/197 (0.51%)
Fatigue [A] *	1/197 (0.51%)
Ill-defined disorder [A] *	1/197 (0.51%)
Pyrexia [A] *	1/197 (0.51%)
Hepatobiliary disorders	
Hepatic failure [A] *	1/197 (0.51%)
Immune system disorders	

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Anaphylactic shock [A] *	1/197 (0.51%)
Drug hypersensitivity [A] *	1/197 (0.51%)
Hypersensitivity [A] *	3/197 (1.52%)
Infections and infestations	
Abscess [A] *	1/197 (0.51%)
Bronchitis [A] *	1/197 (0.51%)
Pneumonia [A] *	3/197 (1.52%)
Psoas abscess [A] *	1/197 (0.51%)
Renal abscess [A] *	1/197 (0.51%)
Sepsis [A] *	1/197 (0.51%)
Tuberculosis [A] *	1/197 (0.51%)
Injury, poisoning and procedural complications	
Rib fracture [A] *	1/197 (0.51%)
Metabolism and nutrition disorders	
Cachexia [A] *	2/197 (1.02%)
Hyperglycaemia [A] *	1/197 (0.51%)
Musculoskeletal and connective tissue disorders	
Pain in extremity [A] *	1/197 (0.51%)
Nervous system disorders	
Hemiparesis [A] *	1/197 (0.51%)
Neuropathy peripheral [A] *	1/197 (0.51%)
Neurotoxicity [A] *	1/197 (0.51%)
Syncope [A] *	1/197 (0.51%)

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Transient ischaemic attack [A] *	1/197 (0.51%)
Renal and urinary disorders	
Hydronephrosis [A] *	1/197 (0.51%)
Renal failure [A] *	1/197 (0.51%)
Renal failure acute [A] *	1/197 (0.51%)
Renal vein thrombosis [A] *	1/197 (0.51%)
Reproductive system and breast disorders	
Genital haemorrhage [A] *	1/197 (0.51%)
Respiratory, thoracic and mediastinal disorders	
Dyspnoea [A] *	1/197 (0.51%)
Laryngeal obstruction [A] *	1/197 (0.51%)
Pulmonary embolism [A] *	7/197 (3.55%)
Surgical and medical procedures	
Vertebroplasty [A] *	1/197 (0.51%)
Vascular disorders	
Deep vein thrombosis [A] *	2/197 (1.02%)
Hypertension [A] *	1/197 (0.51%)
Hypertensive crisis [A] *	3/197 (1.52%)

* 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+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Total	179/197 (90.86%)
Blood and lymphatic system disorders	
Anaemia [A] *	11/197 (5.58%)
Leukopenia [A] *	13/197 (6.6%)
Neutropenia [A] *	32/197 (16.24%)
Thrombocytopenia [A] *	26/197 (13.2%)
Cardiac disorders	
Atrial fibrillation [A] *	1/197 (0.51%)
Cardiac ventricular disorder [A] *	1/197 (0.51%)
Palpitations [A] *	2/197 (1.02%)
Tachycardia [A] *	2/197 (1.02%)
Congenital, familial and genetic disorders	
Dihydropyrimidine dehydrogenase deficiency [A] *	1/197 (0.51%)
Ear and labyrinth disorders	
Deafness [A] *	1/197 (0.51%)
Ear pain [A] *	1/197 (0.51%)
Hypoacusis [A] *	1/197 (0.51%)
Tinnitus [A] *	1/197 (0.51%)
Vertigo [A] *	8/197 (4.06%)
Eye disorders	
Conjunctivitis [A] *	3/197 (1.52%)

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Diplopia [A] *	1/197 (0.51%)
Eye irritation [A] *	1/197 (0.51%)
Eye pain [A] *	1/197 (0.51%)
Lacrimation increased [A] *	1/197 (0.51%)
Scleral haemorrhage [A] *	1/197 (0.51%)
Gastrointestinal disorders	
Abdominal distension [A] *	2/197 (1.02%)
Abdominal hernia [A] *	1/197 (0.51%)
Abdominal pain [A] *	29/197 (14.72%)
Abdominal pain upper [A] *	12/197 (6.09%)
Anal haemorrhage [A] *	1/197 (0.51%)
Anal inflammation [A] *	1/197 (0.51%)
Anorectal discomfort [A] *	2/197 (1.02%)
Constipation [A] *	27/197 (13.71%)
Dental discomfort [A] *	1/197 (0.51%)
Diarrhoea [A] *	73/197 (37.06%)
Dry mouth [A] *	1/197 (0.51%)
Dyspepsia [A] *	4/197 (2.03%)
Dysphagia [A] *	1/197 (0.51%)
Enteritis [A] *	1/197 (0.51%)
Enterocolitis haemorrhage [A] *	1/197 (0.51%)
Flatulence [A] *	2/197 (1.02%)

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Gastritis [A] *	1/197 (0.51%)
Gastrointestinal pain [A] *	1/197 (0.51%)
Gastrointestinal toxicity [A] *	1/197 (0.51%)
Gingival bleeding [A] *	3/197 (1.52%)
Gingivitis [A] *	1/197 (0.51%)
Haematochezia [A] *	1/197 (0.51%)
Haemorrhoidal haemorrhage [A] *	1/197 (0.51%)
Haemorrhoids [A] *	4/197 (2.03%)
Inguinal hernia [A] *	1/197 (0.51%)
Mouth haemorrhage [A] *	1/197 (0.51%)
Nausea [A] *	84/197 (42.64%)
Proctalgia [A] *	3/197 (1.52%)
Rectal haemorrhage [A] *	7/197 (3.55%)
Rectal tenesmus [A] *	1/197 (0.51%)
Stomatitis [A] *	10/197 (5.08%)
Subileus [A] *	1/197 (0.51%)
Tooth disorder [A] *	1/197 (0.51%)
Vomiting [A] *	48/197 (24.37%)
General disorders	
Asthenia [A] *	60/197 (30.46%)
Chest pain [A] *	5/197 (2.54%)
Discomfort [A] *	1/197 (0.51%)

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Facial pain [A] *	1/197 (0.51%)
Fatigue [A] *	29/197 (14.72%)
Hyperpyrexia [A] *	2/197 (1.02%)
Infusion site extravasation [A] *	1/197 (0.51%)
Infusion site pain [A] *	2/197 (1.02%)
Injection site haematoma [A] *	1/197 (0.51%)
Mucosal inflammation [A] *	21/197 (10.66%)
Oedema [A] *	1/197 (0.51%)
Oedema peripheral [A] *	7/197 (3.55%)
Pain [A] *	2/197 (1.02%)
Performance status decreased [A] *	1/197 (0.51%)
Pyrexia [A] *	40/197 (20.3%)
Hepatobiliary disorders	
Hepatomegaly [A] *	2/197 (1.02%)
Hepatotoxicity [A] *	1/197 (0.51%)
Hyperbilirubinaemia [A] *	6/197 (3.05%)
Hypertransaminasaemia [A] *	2/197 (1.02%)
Immune system disorders	
Drug hypersensitivity [A] *	4/197 (2.03%)
Hypersensitivity [A] *	4/197 (2.03%)
Infections and infestations	
Bronchitis [A] *	2/197 (1.02%)

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Cystitis [A] *	2/197 (1.02%)
Ear infection [A] *	1/197 (0.51%)
Folliculitis [A] *	1/197 (0.51%)
Fungal infection [A] *	2/197 (1.02%)
Herpes virus infection [A] *	1/197 (0.51%)
Infection [A] *	1/197 (0.51%)
Influenza [A] *	4/197 (2.03%)
Labyrinthitis [A] *	1/197 (0.51%)
Pharyngitis [A] *	1/197 (0.51%)
Pneumonia [A] *	1/197 (0.51%)
Psoas abscess [A] *	1/197 (0.51%)
Rhinitis [A] *	5/197 (2.54%)
Tooth abscess [A] *	2/197 (1.02%)
Urinary tract infection [A] *	5/197 (2.54%)
Injury, poisoning and procedural complications	
Fall [A] *	1/197 (0.51%)
Foot fracture [A] *	1/197 (0.51%)
Gastrointestinal stoma complications [A] *	1/197 (0.51%)
Wrist fracture [A] *	1/197 (0.51%)
Investigations	
Alanine aminotransferase increased [A] *	5/197 (2.54%)
Aspartate aminotransferase increased [A] *	7/197 (3.55%)

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Blood alkaline phosphatase increased [A] *	3/197 (1.52%)
Blood bilirubin increased [A] *	2/197 (1.02%)
Blood creatinine increased [A] *	1/197 (0.51%)
Blood iron decreased [A] *	1/197 (0.51%)
Blood lactate dehydrogenase increased [A] *	4/197 (2.03%)
Blood uric acid increased [A] *	1/197 (0.51%)
Haemoglobin decreased [A] *	4/197 (2.03%)
Weight decreased [A] *	8/197 (4.06%)
Weight increased [A] *	1/197 (0.51%)
Metabolism and nutrition disorders	
Anorexia [A] *	18/197 (9.14%)
Cachexia [A] *	1/197 (0.51%)
Decreased appetite [A] *	1/197 (0.51%)
Dehydration [A] *	1/197 (0.51%)
Gout [A] *	1/197 (0.51%)
Hypercalcaemia [A] *	1/197 (0.51%)
Hypercholesterolaemia [A] *	1/197 (0.51%)
Hyperglycaemia [A] *	3/197 (1.52%)
Hyperkalaemia [A] *	1/197 (0.51%)
Hypertriglyceridaemia [A] *	1/197 (0.51%)
Hypocalcaemia [A] *	2/197 (1.02%)
Hypokalaemia [A] *	8/197 (4.06%)

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Hypophosphataemia [A] *	1/197 (0.51%)
Musculoskeletal and connective tissue disorders	
Arthralgia [A] *	6/197 (3.05%)
Back pain [A] *	6/197 (3.05%)
Bone pain [A] *	7/197 (3.55%)
Groin pain [A] *	2/197 (1.02%)
Musculoskeletal discomfort [A] *	2/197 (1.02%)
Musculoskeletal pain [A] *	10/197 (5.08%)
Musculoskeletal stiffness [A] *	1/197 (0.51%)
Myalgia [A] *	4/197 (2.03%)
Neck pain [A] *	3/197 (1.52%)
Pain in extremity [A] *	16/197 (8.12%)
Torticollis [A] *	1/197 (0.51%)
Nervous system disorders	
Dizziness [A] *	2/197 (1.02%)
Dysaesthesia [A] *	2/197 (1.02%)
Dysgeusia [A] *	9/197 (4.57%)
Headache [A] *	10/197 (5.08%)
Migraine [A] *	2/197 (1.02%)
Neuralgia [A] *	1/197 (0.51%)
Neuropathy peripheral [A] *	38/197 (19.29%)
Neurotoxicity [A] *	11/197 (5.58%)

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Paraesthesia [A] *	59/197 (29.95%)
Peripheral sensory neuropathy [A] *	5/197 (2.54%)
Presyncope [A] *	1/197 (0.51%)
Sciatica [A] *	1/197 (0.51%)
Syncope [A] *	4/197 (2.03%)
Syncope vasovagal [A] *	1/197 (0.51%)
Tremor [A] *	1/197 (0.51%)
Psychiatric disorders	
Anxiety [A] *	6/197 (3.05%)
Depression [A] *	3/197 (1.52%)
Insomnia [A] *	6/197 (3.05%)
Mood altered [A] *	2/197 (1.02%)
Renal and urinary disorders	
Dysuria [A] *	4/197 (2.03%)
Haematuria [A] *	4/197 (2.03%)
Nocturia [A] *	1/197 (0.51%)
Pollakiuria [A] *	1/197 (0.51%)
Proteinuria [A] *	17/197 (8.63%)
Strangury [A] *	2/197 (1.02%)
Reproductive system and breast disorders	
Balanitis [A] *	1/197 (0.51%)
Genital haemorrhage [A] *	1/197 (0.51%)

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Orchitis noninfective [A] *	1/197 (0.51%)
Testicular disorder [A] *	1/197 (0.51%)
Respiratory, thoracic and mediastinal disorders	
Bronchospasm [A] *	2/197 (1.02%)
Bronchostenosis [A] *	1/197 (0.51%)
Cough [A] *	7/197 (3.55%)
Dysaesthesia pharynx [A] *	4/197 (2.03%)
Dysphonia [A] *	3/197 (1.52%)
Dyspnoea [A] *	12/197 (6.09%)
Epistaxis [A] *	14/197 (7.11%)
Hiccups [A] *	1/197 (0.51%)
Laryngeal disorder [A] *	3/197 (1.52%)
Laryngospasm [A] *	1/197 (0.51%)
Larynx irritation [A] *	2/197 (1.02%)
Oropharyngeal pain [A] *	1/197 (0.51%)
Oropharyngeal spasm [A] *	1/197 (0.51%)
Pharyngeal inflammation [A] *	1/197 (0.51%)
Pleural effusion [A] *	1/197 (0.51%)
Pulmonary embolism [A] *	1/197 (0.51%)
Skin and subcutaneous tissue disorders	
Alopecia [A] *	1/197 (0.51%)
Dermatitis [A] *	1/197 (0.51%)

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Dermatitis exfoliative [A] *	2/197 (1.02%)
Dry skin [A] *	1/197 (0.51%)
Erythema [A] *	3/197 (1.52%)
Hyperhidrosis [A] *	1/197 (0.51%)
Nail disorder [A] *	1/197 (0.51%)
Palmar-plantar erythrodysaesthesia syndrome [A] *	18/197 (9.14%)
Petechiae [A] *	1/197 (0.51%)
Pruritus [A] *	4/197 (2.03%)
Rash [A] *	5/197 (2.54%)
Skin disorder [A] *	1/197 (0.51%)
Skin exfoliation [A] *	2/197 (1.02%)
Skin lesion [A] *	2/197 (1.02%)
Urticaria [A] *	3/197 (1.52%)
Surgical and medical procedures	
Cyst drainage [A] *	1/197 (0.51%)
Vascular disorders	
Aortic thrombosis [A] *	1/197 (0.51%)
Axillary vein thrombosis [A] *	1/197 (0.51%)
Blood pressure fluctuation [A] *	1/197 (0.51%)
Deep vein thrombosis [A] *	5/197 (2.54%)
Hot flush [A] *	1/197 (0.51%)
Hypertension [A] *	45/197 (22.84%)

	Bevacizumab+Oxaliplatin+Capecitabine/Bevacizumab
	Affected/At Risk (%)
Hypertensive crisis [A] *	1/197 (0.51%)
Hypotension [A] *	5/197 (2.54%)
Lymphoedema [A] *	1/197 (0.51%)
Orthostatic hypotension [A] *	1/197 (0.51%)
Phlebitis [A] *	4/197 (2.03%)
Thrombophlebitis [A] *	1/197 (0.51%)
Thrombophlebitis superficial [A] *	1/197 (0.51%)
Thrombosis [A] *	2/197 (1.02%)
Vena cava thrombosis [A] *	1/197 (0.51%)

* 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 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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