ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 01/07/2015

A Study of Bevacizumab (Avastin) in Combination With Capecitabine (Xeloda) in Elderly Patients With Metastatic Colorectal Cancer

This study has been completed.

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT00484939

Purpose

This 2-arm study assessed the efficacy and safety of bevacizumab (Avastin) in combination with capecitabine (Xeloda), compared with capecitabine alone, in elderly patients with metastatic colorectal cancer. Patients were randomized to receive either bevacizumab (7.5 mg/kg intravenously on Day 1 of each 3-week cycle) in combination with capecitabine (1000 mg/m^2 orally twice a day on Days 1-14 of each 3-week cycle) or capecitabine (1000 mg/m^2 orally twice a day on Days 1-14 of each 3-week cycle) alone.

No notable trends or interactions in laboratory values, electrocardiogram, or vital signs suggesting an effect in either direction for capecitabine/bevacizumab combination therapy or capecitabine monotherapy were observed during the study.

Condition	Intervention	Phase
Colorectal Cancer	Drug: Bevacizumab Drug: Capecitabine	Phase 3

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study
Official Title: A Randomised, Open-label Phase III Study to Assess Efficacy and Safety of Bevacizumab in Combination With Capecitabine as First-line Treatment for Elderly Patients With Metastatic Colorectal Cancer

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Progression-free Survival [Time Frame: Baseline to the end of the study (up to 5 years 8 months)] [Designated as safety issue: No]
  Progression-free survival was defined as the time in months from the date of randomization to the date of disease progression or death from any cause, whichever occurred first. All measurable lesions (maximum of 5 per organ and 10 in total, those with the longest diameter and suitability for accurate repeated measurements) were identified as target lesions (TL). A sum of the longest diameter for all TLs was calculated and reported as the baseline sum longest diameter (SLD). All other lesions were identified as non-TLs and recorded at baseline. PD was defined as ≥ 20% increase in the sum of the longest diameter of TLs, taking as reference the smallest SLD recorded since treatment started, the unequivocal progression of existing non-TLs, or the appearance of 1 or more new lesions.

Secondary Outcome Measures:

- Best Overall Response (BOR) [Time Frame: Baseline to the end of the study (up to 5 years 8 months)] [Designated as safety issue: No]
  BOR was defined as the best response (complete response [CR], partial response [PR], stable disease [SD], progressive disease [PD], not evaluable [NE], or not assessed [NA]) recorded from the start of study treatment until disease progression (PD) or death. CR was defined as the disappearance of all target (TL) and non-target lesions (non-TL). PR was defined as ≥ 30% decrease in the sum of the longest diameter (SLD) of TLs, taking as reference the baseline SLD, or the persistence of 1 or more non-TLs. For TLs, SD was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest SLD since treatment started. For non-TLs, SD was defined as the persistence of 1 or more lesions. PD was defined as ≥ 20% increase in the sum of the longest diameter of TLs, taking as reference the smallest SLD recorded since treatment started, the unequivocal progression of existing non-TLs, or the appearance of 1 or more new lesions.
- Duration of Response [Time Frame: Baseline to the end of the study (up to 5 years 8 months)] [Designated as safety issue: No]
  Duration of response was defined as the time in months from the first confirmed complete response (CR) or partial response (PR) until disease progression or death from any cause, whichever occurred first. CR was defined as the disappearance of all target (TL) and non-target lesions (non-TL). PR was defined as ≥ 30% decrease in the sum of the longest diameter (SLD) of TLs, taking as reference the baseline SLD, or the persistence of 1 or more non-TLs.
- Time to Response [Time Frame: Baseline to the end of the study (up to 5 years 8 months)] [Designated as safety issue: No]
  Time to response was defined as the time in months from the date of first study treatment to the date of the first documentation of complete response (CR) or partial response (PR), whichever occurred first. CR was defined as the disappearance of all target (TL) and non-target lesions (non-TL). PR was defined as ≥ 30% decrease in the sum of the longest diameter (SLD) of TLs, taking as reference the baseline SLD, or the persistence of 1 or more non-TLs. Participants who did not have a confirmed response were censored at the date of the last evaluable tumor assessment, or if that was unavailable, at the date of the first dose of study medication.
- Overall Survival [Time Frame: Baseline to the end of the study (up to 5 years 8 months)] [Designated as safety issue: No]
  Overall survival was defined as the time in months from randomization to death from any cause.
- Eastern Cooperative Oncology Group (ECOG) Performance Status [Time Frame: Baseline to the Safety Follow-up which occurred 28 days after the last dose of treatment (up to 5 years 8 months).] [Designated as safety issue: No]
  The ECOG performance status is a scale used to quantify cancer patients' general well-being and activities of daily life. The scale ranges from 0 to 5, with 0 denoting perfect health and 5 indicating death. The 6 categories are 0=Asymptomatic (Fully active, able to carry on all predisease activities without restriction), 1=Symptomatic but completely ambulatory (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature), 2=Symptomatic, < 50% in bed during the day (Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours), 3=Symptomatic, > 50% in bed, but not bedbound (Capable of only limited self-care, confined to bed or chair 50% or more of waking hours), 4=Bedbound (Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair), 5=Death. Reported is the percentage of participants in each of the 6 ECOG performance status categories.
- Percentage of Participants Requiring Additional Treatment for Malignancy [Time Frame: Baseline to the end of the study (up to 5 years 8 months)] [Designated as safety issue: No]
  Reported is the percentage of participants requiring additional treatment for malignancy in the survival follow-up period.
- Duration of Follow-up [Time Frame: Baseline to the end of the study (up to 5 years 8 months)] [Designated as safety issue: No]

Duration of follow-up is defined as the time in days from randomization until disease progression or death, or time to censoring for overall survival.

- AEs, Laboratory Parameters, Vital Signs [Time Frame: Throughout study] [Designated as safety issue: No]

Enrollment: 280
Study Start Date: July 2007
Primary Completion Date: March 2013
Study Completion Date: March 2013

Arms	Assigned Interventions
Experimental: Bevacizumab + capecitabine Participants received bevacizumab 7.5 mg/kg intravenously on Day 1 of each 3-week treatment cycle. In addition, participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.	Drug: Bevacizumab Treatment continued until unacceptable toxicity, withdrawal of consent, disease progression, or a decision to terminate at the discretion of the Investigator if medically indicated. Bevacizumab was supplied in single-use vials. Other Names: Avastin Drug: Capecitabine Treatment continued until unacceptable toxicity, withdrawal of consent, disease progression, or a decision to terminate at the discretion of the Investigator if medically indicated. Capecitabine was supplied as tablets. Other Names: Xeloda
Active Comparator: Capecitabine Participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.	Drug: Capecitabine Treatment continued until unacceptable toxicity, withdrawal of consent, disease progression, or a decision to terminate at the discretion of the Investigator if medically indicated. Capecitabine was supplied as tablets. Other Names: Xeloda

Eligibility

Ages Eligible for Study: 70 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Adult patients, ≥ 70 years of age.
- Cancer of the colon or rectum.
- Metastatic disease diagnosed ≤ 6 months before enrollment.
- ≥ 1 measurable metastatic lesion.

Exclusion Criteria:

- Adjuvant anti-vascular endothelial growth factor (VEGF) treatment.
- Prior chemotherapeutic treatment for metastatic colorectal cancer.
- Past or current history of other malignancies (with the exception of basal and squamous cell cancer of the skin, or in situ cancer of the cervix).
- Clinically significant cardiovascular disease.
- Current or recent daily use of aspirin (> 325 mg/day) or other non-steroidal anti-inflammatory drug (NSAID), or full dose anticoagulants.

Contacts and Locations

Locations

Austria
- Innsbruck, Austria, 6020
- Linz, Austria, 4010
- Salzburg, Austria, 5020
- Wien, Austria, 1220
- Wien, Austria, 1160

Canada, Alberta
- Calgary, Alberta, Canada, T2N 4N2

Canada, British Columbia
- Vancouver, British Columbia, Canada, V5Z 4E6

Canada, Nova Scotia
- Halifax, Nova Scotia, Canada, B3H 2Y9

Canada, Ontario
- London, Ontario, Canada, N6A 4L6
- Ottawa, Ontario, Canada, K1H 8L6
- Toronto, Ontario, Canada, M4N 3M5
- Toronto, Ontario, Canada, M5B 1W8

Canada, Quebec
- Montreal, Quebec, Canada, H3T 1E2

Greece
- Larissa, Greece, 41 110
- Piraeus, Greece, 18537

Hungary
- Budapest, Hungary, 1122
- Budapest, Hungary, 1083
- Gyor, Hungary, 9023
- Zalaegerszeg-Pozva, Hungary, 8900

Italy
- Reggio Emilia, Emilia-Romagna, Italy, 42100
- Roma, Lazio, Italy, 00144
- Lecce, Puglia, Italy, 73100
- Firenze, Toscana, Italy, 50139

Korea, Republic of
- Gyeonggi-do, Korea, Republic of, 410-769
- Incheon, Korea, Republic of, 405-760
- Seoul, Korea, Republic of, 135-710
- Seoul, Korea, Republic of, 110-744

Mexico
- Leon, Mexico, 37000
- Mexico City, Mexico, 16200
- Mexico City, Mexico, 14000
- Mexico City, Mexico, 14140
- Puebla, Mexico, 72530

Netherlands
- Apeldoorn, Netherlands, 7334 DZ
- Eindhoven, Netherlands, 5623 EJ
- Utrecht, Netherlands, 3527 CE

Poland
- Krakow, Poland, 30-501
- Krakow, Poland, 31-826
- Warszawa, Poland, 02-097

Slovenia
- Ljubljana, Slovenia, 1000

Spain
- Barcelona, Barcelona, Spain, 08041
- Jaen, Jaen, Spain, 23007
- Las Palmas de Gran Canaria, Las Palmas, Spain, 35016
- Leganes, Madrid, Spain, 28911
- Madrid, Madrid, Spain, 28040
- Murcia, Murcia, Spain, 30120
- Zaragoza, Zaragoza, Spain, 50009

United Kingdom
- Bristol, United Kingdom, BS2 8ED
- Colchester, United Kingdom, CO3 3NB
- Glasgow, United Kingdom, G12 0YN
- Leicester, United Kingdom, LE1 5WW
- London, United Kingdom, W2 1NY
- Manchester, United Kingdom, M20 4BX
- Nottingham, United Kingdom, NG5 1PB
- Rhyl, United Kingdom, LL18 5UJ
- Sutton, United Kingdom, SM2 5PT

Investigators

Study Director:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party: Hoffmann-La Roche
Study ID Numbers: MO19286
Health Authority: Hungary: Ministry of Health

Study Results

Participant Flow

Reporting Groups

	Description
Bevacizumab + Capecitabine	Participants received bevacizumab 7.5 mg/kg intravenously on Day 1 of each 3-week treatment cycle. In addition, participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.
Capecitabine	Participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.

Overall Study

	Bevacizumab + Capecitabine	Capecitabine
Started	140	140
Completed	0	0
Not Completed	140	140
Death	9	13
Adverse Event	22	12
Patient Withdrew Consent	19	10
Protocol Violation	3	3
Lost to Follow-up	0	3
Discretion of Investigator or Sponsor	7	3
Disease progression	67	88

	Bevacizumab + Capecitabine	Capecitabine
Screen Failure	2	2
Reason Not Specified	11	6

Baseline Characteristics

Analysis Population Description

Intent-to-treat population: All participants randomized into the study.

Reporting Groups

	Description
Bevacizumab + Capecitabine	Participants received bevacizumab 7.5 mg/kg intravenously on Day 1 of each 3-week treatment cycle. In addition, participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.
Capecitabine	Participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.

Baseline Measures

	Bevacizumab + Capecitabine	Capecitabine	Total
Number of Participants	140	140	280
Age, Continuous [units: years] Mean (Standard Deviation)	76.1 (4.18)	76.5 (3.91)	76.3 (4.04)
Gender, Male/Female [units: participants]			
Female	56	56	112
Male	84	84	168

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Progression-free Survival

Measure Description	Progression-free survival was defined as the time in months from the date of randomization to the date of disease progression or death from any cause, whichever occurred first. All measurable lesions (maximum of 5 per organ and 10 in total, those with the longest diameter and suitability for accurate repeated measurements) were identified as target lesions (TL). A sum of the longest diameter for all TLs was calculated and reported as the baseline sum longest diameter (SLD). All other lesions were identified as non-TLs and recorded at baseline. PD was defined as ≥ 20% increase in the sum of the longest diameter of TLs, taking as reference the smallest SLD recorded since treatment started, the unequivocal progression of existing non-TLs, or the appearance of 1 or more new lesions.
Time Frame	Baseline to the end of the study (up to 5 years 8 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population: All participants randomized into the study.

Reporting Groups

	Description
Bevacizumab + Capecitabine	Participants received bevacizumab 7.5 mg/kg intravenously on Day 1 of each 3-week treatment cycle. In addition, participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.
Capecitabine	Participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.

Measured Values

	Bevacizumab + Capecitabine	Capecitabine
Number of Participants Analyzed	140	140
Progression-free Survival [units: Months] Median (95% Confidence Interval)	9.1 (7.3 to 11.3)	5.1 (4.3 to 6.3)

Statistical Analysis 1 for Progression-free Survival

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

Statistical Test of Hypothesis	P-Value	<0.001
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

2. Secondary Outcome Measure:

Measure Title	Best Overall Response (BOR)
Measure Description	BOR was defined as the best response (complete response [CR], partial response [PR], stable disease [SD], progressive disease [PD], not evaluable [NE], or not assessed [NA]) recorded from the start of study treatment until disease progression (PD) or death. CR was defined as the disappearance of all target (TL) and non-target lesions (non-TL). PR was defined as ≥ 30% decrease in the sum of the longest diameter (SLD) of TLs, taking as reference the baseline SLD, or the persistence of 1 or more non-TLs. For TLs, SD was defined as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest SLD since treatment started. For non-TLs, SD was defined as the persistence of 1 or more lesions. PD was defined as ≥ 20% increase in the sum of the longest diameter of TLs, taking as reference the smallest SLD recorded since treatment started, the unequivocal progression of existing non-TLs, or the appearance of 1 or more new lesions.
Time Frame	Baseline to the end of the study (up to 5 years 8 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population: All participants randomized into the study. Only participants with a response were included in the analysis.

Reporting Groups

	Description
Bevacizumab + Capecitabine	Participants received bevacizumab 7.5 mg/kg intravenously on Day 1 of each 3-week treatment cycle. In addition, participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.
Capecitabine	Participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.

Measured Values

	Bevacizumab + Capecitabine	Capecitabine
Number of Participants Analyzed	140	140
Best Overall Response (BOR) [units: Percentage of participants] Number (95% Confidence Interval)		

	Bevacizumab + Capecitabine	Capecitabine
Complete Response	2.9 (0.8 to 7.2)	1.4 (0.2 to 5.1)
Partial Response	17.1 (11.3 to 24.4)	8.6 (4.5 to 14.5)
Stable Disease	54.3 (45.7 to 62.7)	48.6 (40.0 to 57.2)
Progressive Disease	10.0 (5.6 to 16.2)	21.4 (14.9 to 29.2)
Not assessed	15.7 (10.1 to 22.8)	20.0 (13.7 to 27.6)

Statistical Analysis 1 for Best Overall Response (BOR)

Statistical Analysis Overview	Comparison Groups	Bevacizumab + Capecitabine, Capecitabine
	Comments	This statistical analysis compared the number of responders in the 2 treatment groups. A responder was defined as any participant with a best overall response of complete response or partial response. There were 28 responders in the bevacizumab + capecitabine group and 14 responders in the capecitabine group.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.029
	Comments	[Not specified]
	Method	Fisher Exact
	Comments	[Not specified]

3. Secondary Outcome Measure:

Measure Title	Duration of Response
Measure Description	Duration of response was defined as the time in months from the first confirmed complete response (CR) or partial response (PR) until disease progression or death from any cause, whichever occurred first. CR was defined as the disappearance of all target (TL) and non-target lesions (non-TL). PR was defined as ≥ 30% decrease in the sum of the longest diameter (SLD) of TLs, taking as reference the baseline SLD, or the persistence of 1 or more non-TLs.
Time Frame	Baseline to the end of the study (up to 5 years 8 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population: All participants randomized into the study. Only participants with a complete response or partial response were included in the analysis.

Reporting Groups

	Description
Bevacizumab + Capecitabine	Participants received bevacizumab 7.5 mg/kg intravenously on Day 1 of each 3-week treatment cycle. In addition, participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.
Capecitabine	Participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.

Measured Values

	Bevacizumab + Capecitabine	Capecitabine
Number of Participants Analyzed	28	14
Duration of Response [units: Months] Median (95% Confidence Interval)	9.7 (8.3 to 10.9)	9.4 (6.2 to 12.6)

4. Secondary Outcome Measure:

Measure Title	Time to Response
Measure Description	Time to response was defined as the time in months from the date of first study treatment to the date of the first documentation of complete response (CR) or partial response (PR), whichever occurred first. CR was defined as the disappearance of all target (TL) and non-target lesions (non-TL). PR was defined as ≥ 30% decrease in the sum of the longest diameter (SLD) of TLs, taking as reference the baseline SLD, or the persistence of 1 or more non-TLs. Participants who did not have a confirmed response were censored at the date of the last evaluable tumor assessment, or if that was unavailable, at the date of the first dose of study medication.
Time Frame	Baseline to the end of the study (up to 5 years 8 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population: All participants randomized into the study.

Reporting Groups

	Description
Bevacizumab + Capecitabine	Participants received bevacizumab 7.5 mg/kg intravenously on Day 1 of each 3-week treatment cycle. In addition, participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.
Capecitabine	Participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.

Measured Values

	Bevacizumab + Capecitabine	Capecitabine
Number of Participants Analyzed	140	140
Time to Response [units: Months] Median (95% Confidence Interval)	NA (NA to NA) [1]	NA (30.4 to NA) [2]

[1] The median and the lower and upper limits of the 95% confidence interval could not be calculated due to insufficient data.
[2] The median and the upper limit of the 95% confidence interval could not be calculated due to insufficient data.

5. Secondary Outcome Measure:

Measure Title	Overall Survival
Measure Description	Overall survival was defined as the time in months from randomization to death from any cause.
Time Frame	Baseline to the end of the study (up to 5 years 8 months)
Safety Issue?	No

Analysis Population Description
Intent-to-treat population: All participants randomized into the study.

Reporting Groups

	Description
Bevacizumab + Capecitabine	Participants received bevacizumab 7.5 mg/kg intravenously on Day 1 of each 3-week treatment cycle. In addition, participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.
Capecitabine	Participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.

Measured Values

	Bevacizumab + Capecitabine	Capecitabine
Number of Participants Analyzed	140	140
Overall Survival [units: Months] Median (95% Confidence Interval)	20.7 (16.6 to 26.0)	17.0 (12.9 to 22.0)

Statistical Analysis 1 for Overall Survival

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

Statistical Test of Hypothesis	P-Value	0.130
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

6. Secondary Outcome Measure:

Measure Title	Eastern Cooperative Oncology Group (ECOG) Performance Status
Measure Description	The ECOG performance status is a scale used to quantify cancer patients' general well-being and activities of daily life. The scale ranges from 0 to 5, with 0 denoting perfect health and 5 indicating death. The 6 categories are 0=Asymptomatic (Fully active, able to carry on all predisease activities without restriction), 1=Symptomatic but completely ambulatory (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature), 2=Symptomatic, < 50% in bed during the day (Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours), 3=Symptomatic, > 50% in bed, but not bedbound (Capable of only limited self-care, confined to bed or chair 50% or more of waking hours), 4=Bedbound (Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair), 5=Death. Reported is the percentage of participants in each of the 6 ECOG performance status categories.
Time Frame	Baseline to the Safety Follow-up which occurred 28 days after the last dose of treatment (up to 5 years 8 months).
Safety Issue?	No

Analysis Population Description

Intent-to-treat population: All participants randomized into the study.

Reporting Groups

	Description
Bevacizumab + Capecitabine	Participants received bevacizumab 7.5 mg/kg intravenously on Day 1 of each 3-week treatment cycle. In addition, participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.
Capecitabine	Participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.

Measured Values

	Bevacizumab + Capecitabine	Capecitabine
Number of Participants Analyzed	140	140
Eastern Cooperative Oncology Group (ECOG) Performance Status [units: Percentage of participants]		
Week 7 ECOG = 0 (n=117,110)	50.4	34.5
Week 7 ECOG = 1	47.0	58.2
Week 7 ECOG = 2	1.7	5.5
Week 7 ECOG = 3	0.9	1.8
Week 7 ECOG = 4	0.0	0.0
Week 7 ECOG = 5	0.0	0.0
Week 16 ECOG = 0 (n=88,77)	50.0	36.4
Week 16 ECOG = 1	45.5	51.9
Week 16 ECOG = 2	3.4	11.7
Week 16 ECOG = 3	1.1	0.0
Week 16 ECOG = 4	0.0	0.0
Week 16 ECOG = 5	0.0	0.0
Week 25 ECOG = 0 (n=66,42)	43.9	45.2
Week 25 ECOG = 1	48.5	45.2
Week 25 ECOG = 2	6.1	9.5
Week 25 ECOG = 3	1.5	0.0
Week 25 ECOG = 4	0.0	0.0

	Bevacizumab + Capecitabine	Capecitabine
Week 25 ECOG = 5	0.0	0.0
Week 34 ECOG = 0 (n=48,24)	39.6	33.3
Week 34 ECOG = 1	58.3	58.3
Week 34 ECOG = 2	0.0	8.3
Week 34 ECOG = 3	2.1	0.0
Week 34 ECOG = 4	0.0	0.0
Week 34 ECOG = 5	0.0	0.0
Safety Follow-up ECOG = 0 (n=89,82)	33.7	32.9
Safety Follow-up ECOG = 1	47.2	45.1
Safety Follow-up ECOG = 2	12.4	14.6
Safety Follow-up ECOG = 3	6.7	4.9
Safety Follow-up ECOG = 4	0.0	1.2
Safety Follow-up ECOG = 5	0.0	1.2

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants Requiring Additional Treatment for Malignancy
Measure Description	Reported is the percentage of participants requiring additional treatment for malignancy in the survival follow-up period.
Time Frame	Baseline to the end of the study (up to 5 years 8 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population: All participants randomized into the study.

Reporting Groups

	Description
Bevacizumab + Capecitabine	Participants received bevacizumab 7.5 mg/kg intravenously on Day 1 of each 3-week treatment cycle. In addition, participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.

	Description
Capecitabine	Participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.

Measured Values

	Bevacizumab + Capecitabine	Capecitabine
Number of Participants Analyzed	140	140
Percentage of Participants Requiring Additional Treatment for Malignancy [units: Percentage of participants]	50.7	49.3

8. Secondary Outcome Measure:

Measure Title	Duration of Follow-up
Measure Description	Duration of follow-up is defined as the time in days from randomization until disease progression or death, or time to censoring for overall survival.
Time Frame	Baseline to the end of the study (up to 5 years 8 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population: All participants randomized into the study.

Reporting Groups

	Description
Bevacizumab + Capecitabine	Participants received bevacizumab 7.5 mg/kg intravenously on Day 1 of each 3-week treatment cycle. In addition, participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.
Capecitabine	Participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.

Measured Values

	Bevacizumab + Capecitabine	Capecitabine
Number of Participants Analyzed	140	140
Duration of Follow-up [units: Days]	540.5 (423.52)	479.2 (401.01)

	Bevacizumab + Capecitabine	Capecitabine
Mean (Standard Deviation)		

9. Secondary Outcome Measure:

Measure Title	AEs, Laboratory Parameters, Vital Signs
Measure Description	
Time Frame	Throughout study
Safety Issue?	No

Outcome Measure Data Not Reported

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	Safety population: All participants who had at least 1 dose of study medication.

Reporting Groups

	Description
Bevacizumab + Capecitabine	Participants received bevacizumab 7.5 mg/kg intravenously on Day 1 of each 3-week treatment cycle. In addition, participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.
Capecitabine	Participants received capecitabine 1000 mg/m^2 orally twice daily on Days 1-14 of each 3-week treatment cycle.

Serious Adverse Events

	Bevacizumab + Capecitabine	Capecitabine
	Affected/At Risk (%)	Affected/At Risk (%)
Total	40/134 (29.85%)	42/136 (30.88%)
Blood and lymphatic system disorders		
Anaemia [A] †	0/134 (0%)	1/136 (0.74%)
Neutropenia [A] †	0/134 (0%)	1/136 (0.74%)

	Bevacizumab + Capecitabine	Capecitabine
	Affected/At Risk (%)	Affected/At Risk (%)
Cardiac disorders		
Angina pectoris [A] †	1/134 (0.75%)	1/136 (0.74%)
Cardiac arrest [A] †	1/134 (0.75%)	2/136 (1.47%)
Cardiac failure [A] †	0/134 (0%)	1/136 (0.74%)
Myocardial infarction [A] †	1/134 (0.75%)	0/136 (0%)
Myocardial ischaemia [A] †	1/134 (0.75%)	0/136 (0%)
Eye disorders		
Amaurosis fugax [A] †	1/134 (0.75%)	0/136 (0%)
Gastrointestinal disorders		
Abdominal discomfort [A] †	1/134 (0.75%)	0/136 (0%)
Abdominal pain [A] †	3/134 (2.24%)	4/136 (2.94%)
Ascites [A] †	0/134 (0%)	3/136 (2.21%)
Colonic obstruction [A] †	0/134 (0%)	1/136 (0.74%)
Diarrhoea [A] †	0/134 (0%)	4/136 (2.94%)
Haematochezia [A] †	1/134 (0.75%)	0/136 (0%)
Inguinal hernia [A] †	1/134 (0.75%)	0/136 (0%)
Intestinal obstruction [A] †	3/134 (2.24%)	4/136 (2.94%)
Mechanical ileus [A] †	0/134 (0%)	1/136 (0.74%)
Nausea [A] †	1/134 (0.75%)	0/136 (0%)
Small intestinal obstruction [A] †	1/134 (0.75%)	0/136 (0%)
Upper gastrointestinal haemorrhage [A] †	0/134 (0%)	1/136 (0.74%)
Vomiting [A] †	2/134 (1.49%)	2/136 (1.47%)
General disorders		

	Bevacizumab + Capecitabine	Capecitabine
	Affected/At Risk (%)	Affected/At Risk (%)
Asthenia [A] †	0/134 (0%)	1/136 (0.74%)
Death [A] †	1/134 (0.75%)	0/136 (0%)
Fatigue [A] †	0/134 (0%)	1/136 (0.74%)
General physical health deterioration [A] †	1/134 (0.75%)	2/136 (1.47%)
Oedema [A] †	1/134 (0.75%)	0/136 (0%)
Pain [A] †	1/134 (0.75%)	1/136 (0.74%)
Pyrexia [A] †	3/134 (2.24%)	2/136 (1.47%)
Hepatobiliary disorders		
Hepatic failure [A] †	0/134 (0%)	1/136 (0.74%)
Hepatitis acute [A] †	0/134 (0%)	1/136 (0.74%)
Jaundice [A] †	0/134 (0%)	2/136 (1.47%)
Infections and infestations		
Bronchitis [A] †	1/134 (0.75%)	0/136 (0%)
Cellulitis gangrenous [A] †	0/134 (0%)	1/136 (0.74%)
Escherichia urinary tract infection [A] †	1/134 (0.75%)	0/136 (0%)
Gastroenteritis [A] †	0/134 (0%)	1/136 (0.74%)
Lower respiratory tract infection [A] †	1/134 (0.75%)	0/136 (0%)
Pneumonia [A] †	3/134 (2.24%)	1/136 (0.74%)
Pneumonia bacterial [A] †	1/134 (0.75%)	0/136 (0%)
Pulmonary sepsis [A] †	1/134 (0.75%)	0/136 (0%)
Sepsis [A] †	0/134 (0%)	1/136 (0.74%)
Urosepsis [A] †	1/134 (0.75%)	0/136 (0%)

	Bevacizumab + Capecitabine	Capecitabine
	Affected/At Risk (%)	Affected/At Risk (%)
Injury, poisoning and procedural complications		
Excoriation [A] †	1/134 (0.75%)	0/136 (0%)
Impacted fracture [A] †	1/134 (0.75%)	0/136 (0%)
Patella fracture [A] †	1/134 (0.75%)	0/136 (0%)
Spinal compression fracture [A] †	1/134 (0.75%)	0/136 (0%)
Metabolism and nutrition disorders		
Decreased appetite [A] †	0/134 (0%)	2/136 (1.47%)
Dehydration [A] †	1/134 (0.75%)	1/136 (0.74%)
Musculoskeletal and connective tissue disorders		
Groin pain [A] †	1/134 (0.75%)	0/136 (0%)
Neck pain [A] †	0/134 (0%)	1/136 (0.74%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Metastases to lung [A] †	0/134 (0%)	1/136 (0.74%)
Metastatic neoplasm [A] †	1/134 (0.75%)	1/136 (0.74%)
Nervous system disorders		
Amnesia [A] †	1/134 (0.75%)	0/136 (0%)
Cerebral ischaemia [A] †	1/134 (0.75%)	0/136 (0%)
Lethargy [A] †	1/134 (0.75%)	0/136 (0%)
Somnolence [A] †	1/134 (0.75%)	0/136 (0%)
Transient ischaemic attack [A] †	1/134 (0.75%)	1/136 (0.74%)
Renal and urinary disorders		
Calculus ureteric [A] †	1/134 (0.75%)	1/136 (0.74%)
Renal failure [A] †	0/134 (0%)	1/136 (0.74%)

	Bevacizumab + Capecitabine	Capecitabine
	Affected/At Risk (%)	Affected/At Risk (%)
Reproductive system and breast disorders		
Female genital tract fistula [A] †	1/134 (0.75%)	0/136 (0%)
Respiratory, thoracic and mediastinal disorders		
Dyspnoea [A] †	0/134 (0%)	1/136 (0.74%)
Pleural effusion [A] †	1/134 (0.75%)	1/136 (0.74%)
Pulmonary embolism [A] †	8/134 (5.97%)	2/136 (1.47%)
Skin and subcutaneous tissue disorders		
Rash macular [A] †	1/134 (0.75%)	0/136 (0%)
Surgical and medical procedures		
Bone operation [A] †	0/134 (0%)	1/136 (0.74%)
Vascular disorders		
Circulatory collapse [A] †	0/134 (0%)	1/136 (0.74%)
Deep vein thrombosis [A] †	0/134 (0%)	3/136 (2.21%)
Hypertension [A] †	2/134 (1.49%)	1/136 (0.74%)
Peripheral artery thrombosis [A] †	0/134 (0%)	1/136 (0.74%)
Thrombosis [A] †	2/134 (1.49%)	0/136 (0%)
Vena cava thrombosis [A] †	0/134 (0%)	1/136 (0.74%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (12.1)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Bevacizumab + Capecitabine	Capecitabine
	Affected/At Risk (%)	Affected/At Risk (%)
Total	129/134 (96.27%)	130/136 (95.59%)

	Bevacizumab + Capecitabine	Capecitabine
	Affected/At Risk (%)	Affected/At Risk (%)
Blood and lymphatic system disorders		
Neutropenia [A] †	7/134 (5.22%)	2/136 (1.47%)
Gastrointestinal disorders		
Abdominal pain [A] †	31/134 (23.13%)	21/136 (15.44%)
Abdominal pain upper [A] †	11/134 (8.21%)	5/136 (3.68%)
Constipation [A] †	25/134 (18.66%)	19/136 (13.97%)
Diarrhoea [A] †	54/134 (40.3%)	48/136 (35.29%)
Dyspepsia [A] †	9/134 (6.72%)	4/136 (2.94%)
Nausea [A] †	32/134 (23.88%)	37/136 (27.21%)
Stomatitis [A] †	14/134 (10.45%)	14/136 (10.29%)
Vomiting [A] †	28/134 (20.9%)	16/136 (11.76%)
General disorders		
Asthenia [A] †	30/134 (22.39%)	22/136 (16.18%)
Fatigue [A] †	32/134 (23.88%)	37/136 (27.21%)
Mucosal inflammation [A] †	20/134 (14.93%)	11/136 (8.09%)
Oedema peripheral [A] †	11/134 (8.21%)	17/136 (12.5%)
Pain [A] †	11/134 (8.21%)	6/136 (4.41%)
Pyrexia [A] †	24/134 (17.91%)	16/136 (11.76%)
Metabolism and nutrition disorders		
Decreased Appetite [A] †	38/134 (28.36%)	31/136 (22.79%)
Musculoskeletal and connective tissue disorders		
Arthralgia [A] †	12/134 (8.96%)	4/136 (2.94%)
Back pain [A] †	13/134 (9.7%)	11/136 (8.09%)

	Bevacizumab + Capecitabine	Capecitabine
	Affected/At Risk (%)	Affected/At Risk (%)
Musculoskeletal pain [A] †	10/134 (7.46%)	4/136 (2.94%)
Pain in extremity [A] †	11/134 (8.21%)	5/136 (3.68%)
Nervous system disorders		
Dizziness [A] †	9/134 (6.72%)	17/136 (12.5%)
Dysgeusia [A] †	8/134 (5.97%)	6/136 (4.41%)
Headache [A] †	10/134 (7.46%)	5/136 (3.68%)
Lethargy [A] †	12/134 (8.96%)	15/136 (11.03%)
Paraesthesia [A] †	8/134 (5.97%)	1/136 (0.74%)
Psychiatric disorders		
Insomnia [A] †	7/134 (5.22%)	7/136 (5.15%)
Renal and urinary disorders		
Proteinuria [A] †	10/134 (7.46%)	1/136 (0.74%)
Respiratory, thoracic and mediastinal disorders		
Cough [A] †	15/134 (11.19%)	12/136 (8.82%)
Dyspnoea [A] †	12/134 (8.96%)	13/136 (9.56%)
Epistaxis [A] †	23/134 (17.16%)	5/136 (3.68%)
Pulmonary embolism [A] †	9/134 (6.72%)	2/136 (1.47%)
Rhinorrhoea [A] †	8/134 (5.97%)	1/136 (0.74%)
Skin and subcutaneous tissue disorders		
Dry skin [A] †	8/134 (5.97%)	4/136 (2.94%)
Palmar-Plantar erythrodysaesthesia syndrome [A] †	66/134 (49.25%)	54/136 (39.71%)
Rash [A] †	6/134 (4.48%)	12/136 (8.82%)

	Bevacizumab + Capecitabine	Capecitabine
	Affected/At Risk (%)	Affected/At Risk (%)
Skin hyperpigmentation [A] †	11/134 (8.21%)	2/136 (1.47%)
Vascular disorders		
Hypertension [A] †	22/134 (16.42%)	6/136 (4.41%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (12.1)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The Study being conducted under this Agreement is part of the Overall Study. Investigator is free to publish in reputable journals or to present at professional conferences the results of the Study, but only after the first publication or presentation that involves the Overall Study. The Sponsor may request that Confidential Information be deleted and/or the publication be postponed in order to protect the Sponsor's intellectual property rights.

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