ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 01/08/2015

A Study of Avastin (Bevacizumab) in Combination Chemotherapy in Patients With Metastatic Cancer of the Colon or Rectum

This study has been completed.

Sponsor:	Hoffmann-La Roche
Collaborators:	
Information provided by (Responsible Party):	Hoffmann-La Roche
ClinicalTrials.gov Identifier:	NCT01131078

Purpose

A study of Avastin (bevacizumab) in combination chemotherapy in patients with metastatic cancer of the colon or rectum. The anticipated time on study treatment is until disease progression.

Condition	Intervention	Phase
Colorectal Cancer	Drug: Bevacizumab [Avastin] Drug: Capecitabine Drug: Irinotecan	Phase 2

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Open Label, Randomized, Safety/Efficacy Study
Official Title: A Randomized, Open-label Study Comparing the Effect of 3 Chemotherapy Regimens Containing Avastin on Time to Disease Progression in Patients With Metastatic Colorectal Cancer

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Percentage of Participants With Disease Progression or Death [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]

Disease progression was defined according to National Cancer Institute (NCI) guidelines and best clinical practices.

- Time to Progression (TTP) [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  TTP is defined as the time from date of randomization until objective tumor progression or death due to any cause. It includes deaths and thus can be correlated to overall survival.

Secondary Outcome Measures:

- Percentage of Participants Who Died [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  Overall survival is defined as the time from date of randomization until death from any cause
- Overall Survival [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  Overall survival is defined as the time from date of randomization until death from any cause; Kaplan-Meier estimates were used for analysis.
- Percentage of Participants With Treatment Failure [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  Treatment failure is defined as discontinuation of treatment for any reason, including disease progression, death, treatment toxicity, insufficient therapeutic response, failure to return, refusing treatment, being unwilling to cooperate and withdrawing consent.
- Time to Treatment Failure [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  Time to treatment failure is defined as a composite endpoint measuring time from date of randomization to discontinuation of treatment for any reason, including disease progression, death, treatment toxicity, insufficient therapeutic response, failure to return, refusing treatment, being unwilling to cooperate and withdrawing consent. Analysis was performed using Kaplan-Meier estimates.
- Percentage of Participants With Progression Excluding Deaths [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  The failure event was defined as tumor progression excluding deaths due to any reason.
- Time to Progression Excluding Deaths [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  The failure event was defined as tumor progression excluding deaths due to any reason. Kaplan-Meier estimates were used for analysis.
- Percentage of Participants With Progression Excluding Deaths Not Related to Underlying Cancer [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  The failure event was defined as tumor progression excluding only deaths not related to underlying cancer.
- Time to Progression Excluding Deaths Not Related to Underlying Cancer [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  The failure event was defined as tumor progression excluding only deaths not related to underlying cancer. Kaplan-Meier estimates were used for analysis.
- Percentage of Participants by Best Overall Response [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  Best overall response is defined as the best response recorded from the date of randomization until disease progression or recurrence. Complete response (CR): at least 2 determinations of CR at least 4 weeks apart before progression; Partial response (PR): at least 2 determinations of PR at least 4 weeks apart before progression; Stable disease (SD): at least one SD assessment; Progressive Disease (PD): Disease progression or death due to underlying cancer. CR: Complete disappearance of all target lesions; PR: At least 30% decrease in the sum of the longest diameter of all target lesions taking as reference the baseline sum of all target lesions; PD: At least 20% decrease in the sum of the longest diameter of all target lesions taking as reference the baseline sum of longest diameter of all target lesions or the appearance of one or more new lesions; SD: Neither sufficient shrinkage to qualify for CR or PR or increase in lesions;
- Percentage of Participants With a Best Overall Response of CR or PR [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  CR: Complete disappearance of all target lesions; PR: At least 30% decrease in the sum of the longest diameter of all target lesions taking as reference the baseline sum of all target lesions;

- Percentage of Participants With Stable Disease [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  Stable disease rate was the proportion of participants who achieved CR, PR, or SD.
- Percentage of Participants With Progressive Disease Within 12 Weeks From Start of Treatment [Time Frame: Randomization, Weeks 3, 6 and 9, and 12] [Designated as safety issue: No]
  Early progression was the proportion of participants with progressive disease within 12 weeks from the start of treatment.
- Duration of Overall Response [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  Duration of overall response included participants who achieved a CR or PR.
- Duration of Stable Disease (SD) [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death] [Designated as safety issue: No]
  Duration of SD was calculated as the number of months the participants remained in CR, PR or SD. Kaplan-Meier estimates were used for analysis.
- Duration of Overall Complete Response [Time Frame: Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years] [Designated as safety issue: No]
  Duration of complete response was calculated as the time in months from the date of randomization to the date of first documentation of CR. Kaplan-Meier estimates were used for analysis.

Enrollment: 306
Study Start Date: June 2005
Primary Completion Date: November 2012
Study Completion Date: November 2012

Arms	Assigned Interventions
Experimental: Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2) Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.	Drug: Bevacizumab [Avastin] Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Other Names: Avastin Drug: Capecitabine Capecitabine was administered orally at a doses of 1000 or 1250, mg/m^2 twice daily (Day 2 to 15) or as 650 mg/m^2 twice daily on Days 1 to 21. Drug: Irinotecan Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks.
Experimental: Bevacizumab + Capecitabine (1250 mg/m^2)	Drug: Bevacizumab [Avastin]

Arms	Assigned Interventions
Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Other Names: Avastin Drug: Capecitabine Capecitabine was administered orally at a doses of 1000 or 1250, mg/m^2 twice daily (Day 2 to 15) or as 650 mg/m^2 twice daily on Days 1 to 21.
Experimental: Bevacizumab + Capecitabine (650 mg/m^2) Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 Week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of capecitabine treatment without interruptions. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.	Drug: Bevacizumab [Avastin] Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Other Names: Avastin Drug: Capecitabine Capecitabine was administered orally at a doses of 1000 or 1250, mg/m^2 twice daily (Day 2 to 15) or as 650 mg/m^2 twice daily on Days 1 to 21.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- adult patients >=18 years of age;
- colon or rectal cancer, with metastases;
- >=1 measurable lesion.

Exclusion Criteria:

- previous systemic treatment for advanced disease;

- radiotherapy to any site within 4 weeks before study;
- daily aspirin (>325 mg/day), anticoagulants, or other medications known to predispose to gastrointestinal ulceration;
- co-existing malignancies or malignancies diagnosed within last 5 years (except basal cell cancer or cervical cancer in situ).

Contacts and Locations

Locations

Italy

Paola, Calabria, Italy, 87027
Benevento, Campania, Italy, 82100
Napoli, Campania, Italy, 80136
Bologna, Emilia-Romagna, Italy, 40138
Carpi, Emilia-Romagna, Italy, 41012
Piacenza, Emilia-Romagna, Italy, 29100
Latisana, Friuli-Venezia Giulia, Italy, 33053
Udine, Friuli-Venezia Giulia, Italy, 33100
Latina, Lazio, Italy, 04100
Roma, Lazio, Italy, 00168
Roma, Lazio, Italy, 00186
Brescia, Lombardia, Italy, 25123
Busto Arsizio, Lombardia, Italy, 21052
Casalpusterlengo, Lombardia, Italy, 20071
Cremona, Lombardia, Italy, 26100
Gorgonzola, Lombardia, Italy, 20064
Lecco, Lombardia, Italy, 23900
Legnago, Lombardia, Italy, 37045
Mantova, Lombardia, Italy, 46100
Milano, Lombardia, Italy, 20133
Milano, Lombardia, Italy, 20142
Milano, Lombardia, Italy, 20121
Milano, Lombardia, Italy, 20162
Pavia, Lombardia, Italy, 27100
Pavia, Lombardia, Italy, 27100
Saronno, Lombardia, Italy, 21047
Sondrio, Lombardia, Italy, 23100
Treviglio, Lombardia, Italy, 24047
Varese, Lombardia, Italy, 21100
Ancona, Marche, Italy, 60121
Novara, Piemonte, Italy, 28100
Torino, Piemonte, Italy, 10153
Cagliari, Sardegna, Italy, 09100
Catania, Sicilia, Italy, 95100
Palermo, Sicilia, Italy, 90127
Palermo, Sicilia, Italy, 90127

Palermo, Sicilia, Italy, 90127
Firenze, Toscana, Italy, 50139
Firenze, Toscana, Italy, 50139
Grosseto, Toscana, Italy, 58100
Pisa, Toscana, Italy, 56100
Prato, Toscana, Italy, 59100
Bolzano, Trentino-Alto Adige, Italy, 39100
Terni, Umbria, Italy, 05100
Camposampiero, Veneto, Italy, 35012
Este, Veneto, Italy, 35042
Montecchio Maggiore, Veneto, Italy, 36075
Negrar, Veneto, Italy, 37024

Investigators

Study Chair:	Clinical Trials	Hoffmann-La Roche

More Information

Responsible Party:	Hoffmann-La Roche
Study ID Numbers:	ML18524
Health Authority:	ITALY: Agenzia Italiana del Farmaco

Study Results

Participant Flow

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 milligrams per kilogram (mg/kg) intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 milligrams per meter squared (mg/m^2) intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or stable disease (SD) were treated with bevacizumab alone until unacceptable toxicity, progressive disease (PD), or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.

	Description
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 Week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of capecitabine treatment without interruptions. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Overall Study

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Started	101	102	103
Completed	0	1	1
Not Completed	101	101	102
Adverse Event	22	12	17
Progressive Disease	58	77	71
Protocol Violation	1	0	0
Lost to Follow-up	1	1	1
Withdrawal by Subject	2	4	3
Non-compliance	3	0	0
Physician Decision	10	6	8
Death	4	0	2
Unknown	0	1	0

Baseline Characteristics

Analysis Population Description

All enrolled participants were included in the Intent-to-Treat (ITT) population.

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 Week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of capecitabine treatment without interruptions. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Baseline Measures

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)	Total
Number of Participants	101	102	103	306
Age, Continuous [units: years] Mean (Standard Deviation)	61.60 (9.35)	61.46 (10.22)	61.01 (10.10)	61.36 (9.86)
Gender, Male/Female [units: participants]				
Female	58	53	63	174
Male	43	49	40	132

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Percentage of Participants With Disease Progression or Death
Measure Description	Disease progression was defined according to National Cancer Institute (NCI) guidelines and best clinical practices.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description
ITT Population;

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	101	102	103
Percentage of Participants With Disease Progression or Death [units: percentage of participants]	86.14	90.20	88.35

2. Primary Outcome Measure:

Measure Title	Time to Progression (TTP)
Measure Description	TTP is defined as the time from date of randomization until objective tumor progression or death due to any cause. It includes deaths and thus can be correlated to overall survival.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description

ITT Population; only those participants with an event of disease progression or death were included in the analysis

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	87	92	91
Time to Progression (TTP) [units: months] Median (95% Confidence Interval)	8.35 (7.23 to 9.60)	8.15 (6.74 to 8.75)	7.27 (4.57 to 8.98)

3. Secondary Outcome Measure:

Measure Title	Percentage of Participants Who Died
Measure Description	Overall survival is defined as the time from date of randomization until death from any cause
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	101	102	103
Percentage of Participants Who Died [units: percentage of participants]	67.33	71.57	73.79

4. Secondary Outcome Measure:

Measure Title	Overall Survival
Measure Description	Overall survival is defined as the time from date of randomization until death from any cause; Kaplan-Meier estimates were used for analysis.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description

ITT Population; Only participants with an event (death) were included in the analysis.

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	68	73	76
Overall Survival [units: months] Median (95% Confidence Interval)	22.75 (18.94 to 26.63)	19.76 (18.38 to 24.00)	18.02 (14.76 to 20.61)

5. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Treatment Failure
Measure Description	Treatment failure is defined as discontinuation of treatment for any reason, including disease progression, death, treatment toxicity, insufficient therapeutic response, failure to return, refusing treatment, being unwilling to cooperate and withdrawing consent.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	101	102	103
Percentage of Participants With Treatment Failure [units: percentage of participants]	100.0	99.02	99.03

6. Secondary Outcome Measure:

Measure Title	Time to Treatment Failure
Measure Description	Time to treatment failure is defined as a composite endpoint measuring time from date of randomization to discontinuation of treatment for any reason, including disease progression, death, treatment toxicity, insufficient therapeutic response, failure to return, refusing treatment, being unwilling to cooperate and withdrawing consent. Analysis was performed using Kaplan-Meier estimates.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death

Safety Issue?	No

Analysis Population Description

ITT Population; only participants with a treatment failure event were included in the analysis.

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	101	101	102
Time to Treatment Failure [units: months] Median (95% Confidence Interval)	6.67 (5.82 to 7.56)	6.87 (5.49 to 8.38)	5.75 (4.34 to 7.27)

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Progression Excluding Deaths
Measure Description	The failure event was defined as tumor progression excluding deaths due to any reason.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	101	102	103
Percentage of Participants With Progression Excluding Deaths [units: percentage of participants]	71.29	81.37	75.73

8. Secondary Outcome Measure:

Measure Title	Time to Progression Excluding Deaths
Measure Description	The failure event was defined as tumor progression excluding deaths due to any reason. Kaplan-Meier estimates were used for analysis.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description

ITT Population; Only participants with a time to progression event (excluding deaths) were included in the analysis.

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	72	83	78
Time to Progression Excluding Deaths [units: months] Median (95% Confidence Interval)	8.81 (7.66 to 10.82)	8.48 (6.90 to 8.84)	7.40 (4.87 to 9.17)

9. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Progression Excluding Deaths Not Related to Underlying Cancer
Measure Description	The failure event was defined as tumor progression excluding only deaths not related to underlying cancer.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description
ITT Population

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal..
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	101	102	103
Percentage of Participants With Progression Excluding Deaths Not Related to Underlying Cancer [units: percentage of participants]	81.19	90.20	85.44

10. Secondary Outcome Measure:

Measure Title	Time to Progression Excluding Deaths Not Related to Underlying Cancer
Measure Description	The failure event was defined as tumor progression excluding only deaths not related to underlying cancer. Kaplan-Meier estimates were used for analysis.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description

ITT Population; only participants with a time to progression event (excluding deaths not related to underlying cancer) were included in the analysis.

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	82	92	88
Time to Progression Excluding Deaths Not Related to Underlying Cancer [units: months] Median (95% Confidence Interval)	8.68 (7.59 to 9.90)	8.32 (6.74 to 8.75)	7.27 (4.57 to 9.11)

11. Secondary Outcome Measure:

Measure Title	Percentage of Participants by Best Overall Response

Measure Description	Best overall response is defined as the best response recorded from the date of randomization until disease progression or recurrence. Complete response (CR): at least 2 determinations of CR at least 4 weeks apart before progression; Partial response (PR): at least 2 determinations of PR at least 4 weeks apart before progression; Stable disease (SD): at least one SD assessment; Progressive Disease (PD): Disease progression or death due to underlying cancer. CR: Complete disappearance of all target lesions; PR: At least 30% decrease in the sum of the longest diameter of all target lesions taking as reference the baseline sum of all target lesions; PD: At least 20% decrease in the sum of the longest diameter of all target lesions taking as reference the baseline sum of longest diameter of all target lesions or the appearance of one or more new lesions; SD: Neither sufficient shrinkage to qualify for CR or PR or increase in lesions;
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description

ITT Population; All participants with evaluable data were included in the analysis

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	91	92	94
Percentage of Participants by Best Overall Response [units: percentage of participants]			

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
CR	5.49	1.09	5.32
PR	46.15	32.61	28.72
SD	39.56	52.17	45.74
PD	8.79	14.13	20.21

12. Secondary Outcome Measure:

Measure Title	Percentage of Participants With a Best Overall Response of CR or PR
Measure Description	CR: Complete disappearance of all target lesions; PR: At least 30% decrease in the sum of the longest diameter of all target lesions taking as reference the baseline sum of all target lesions;
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description

ITT Population; All participants with evaluable data were included in the analysis

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	91	92	94
Percentage of Participants With a Best Overall Response of CR or PR [units: percentage of participants] Number (95% Confidence Interval)	52.0 (41.0 to 62.0)	34.0 (24.0 to 44.0)	34.0 (25.0 to 45.0)

13. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Stable Disease
Measure Description	Stable disease rate was the proportion of participants who achieved CR, PR, or SD.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description

ITT Population; All participants with evaluable data were included in the analysis

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	91	92	94
Percentage of Participants With Stable Disease [units: percentage of participants] Number (95% Confidence Interval)	91.0 (83.0 to 96.0)	86.0 (77.0 to 92.0)	80.0 (70.0 to 87.0)

14. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Progressive Disease Within 12 Weeks From Start of Treatment
Measure Description	Early progression was the proportion of participants with progressive disease within 12 weeks from the start of treatment.
Time Frame	Randomization, Weeks 3, 6 and 9, and 12
Safety Issue?	No

Analysis Population Description

ITT Population; All participants with evaluable data were included in the analysis.

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	91	92	94
Percentage of Participants With Progressive Disease Within 12 Weeks From Start of Treatment [units: percentage of participants] Number (95% Confidence Interval)	9.0 (4.0 to 17.0)	13.0 (7.0 to 22.0)	18.0 (11.0 to 27.0)

15. Secondary Outcome Measure:

Measure Title	Duration of Overall Response
Measure Description	Duration of overall response included participants who achieved a CR or PR.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description

ITT Population; only participants with a best overall response of CR or PR were included in the analysis.

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	47	31	32
Duration of Overall Response [units: months] Median (95% Confidence Interval)	6.51 (5.36 to 8.35)	6.61 (6.15 to 8.28)	9.12 (6.48 to 16.08)

16. Secondary Outcome Measure:

Measure Title	Duration of Stable Disease (SD)
Measure Description	Duration of SD was calculated as the number of months the participants remained in CR, PR or SD. Kaplan-Meier estimates were used for analysis.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years or Death
Safety Issue?	No

Analysis Population Description

ITT Population; Only participants with a best overall response of CR, PR, or SD were included in the analysis.

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	8	79	75
Duration of Stable Disease (SD) [units: months] Median (95% Confidence Interval)	8.81 (7.86 to 10.55)	8.65 (7.99 to 9.34)	8.98 (7.30 to 9.99)

17. Secondary Outcome Measure:

Measure Title	Duration of Overall Complete Response
Measure Description	Duration of complete response was calculated as the time in months from the date of randomization to the date of first documentation of CR. Kaplan-Meier estimates were used for analysis.
Time Frame	Randomization, Weeks 3, 6 and 9, and every 3 months up to 5 years
Safety Issue?	No

Analysis Population Description

ITT Population; Only participants with a best overall response were included in the analysis.

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3-week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of continuous capecitabine treatment. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Measured Values

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
Number of Participants Analyzed	5	1	5
Duration of Overall Complete Response [units: months] Median (95% Confidence Interval)	8.35 (5.16 to NA) [1]	6.05 (NA to NA) [2]	12.89 (7.63 to 33.04)

[1] Upper limit of the 95% confidence interval was not estimable as the duration of follow-up was not sufficient.
[2] Number of participants analyzed for this parameter in this treatment group was 1, therefore 95% CI could not be determined.

Reported Adverse Events

Time Frame	Adverse events were recorded from the date of randomization until the End of Study or until death in safety population. Safety population included all participants who signed informed consent and took at least one dose of each drug of study combination.
Additional Description	[Not specified]

Reporting Groups

	Description
Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle. Irinotecan was administered as a 240 mg/m^2 intravenous infusion over 60 minutes (Day 1) every 3 weeks. Capecitabine was administered orally at a dose of 1000 mg/m^2 twice daily (Day 2 to 15). Cycle length was 3 weeks consisting of 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 week cycle in combination with capecitabine administered orally at 1250 mg/m^2 twice daily (Day 1 to 14). Cycle length was 3 weeks with 2 weeks of capecitabine treatment followed by 1 week without treatment up to 6 cycles. After 6 cycles, participants with objective response or SD were treated with bevacizumab alone until unacceptable toxicity, PD, or participant withdrawal.
Bevacizumab + Capecitabine (650 mg/m^2)	Bevacizumab was administered as a 7.5 mg/kg intravenous infusion over 30 to 90 minutes on Day 1 of each 3 Week cycle in combination with capecitabine administered orally at 650 mg/m^2 twice daily (Day 1 to 21). Cycle length was 3 weeks with 3 weeks of capecitabine treatment without interruptions. Participants received the same regimen until unacceptable toxicity, PD, or participant withdrawal.

Serious Adverse Events

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	38/100 (38%)	21/99 (21.21%)	20/102 (19.61%)
Blood and lymphatic system disorders			
Disseminated intravascular coagulation [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Febrile neutropenia [A] *	3/100 (3%)	0/99 (0%)	0/102 (0%)
Leukopenia [A] *	2/100 (2%)	0/99 (0%)	0/102 (0%)
Neutropenia [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Pancytopenia [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Thrombocytopenia [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Cardiac disorders			
Arrhythmia [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Cardiac failure [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Myocardial infarction [A] *	2/100 (2%)	0/99 (0%)	0/102 (0%)
Myocardial ischemia [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Supraventricular tachycardia [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Gastrointestinal disorders			
Abdominal haematoma [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Abdominal pain [A] *	1/100 (1%)	2/99 (2.02%)	2/102 (1.96%)
Diarrhoea [A] *	7/100 (7%)	1/99 (1.01%)	1/102 (0.98%)
Gastrointestinal disorder [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Intestinal haemorrhage [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Intestinal obstruction [A] *	6/100 (6%)	0/99 (0%)	2/102 (1.96%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Intestinal prolapse [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Nausea [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Pancreatitis [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Rectal haemorrhage [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Subileus [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Swollen tongue [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Vomiting [A] *	1/100 (1%)	1/99 (1.01%)	0/102 (0%)
General disorders			
Chest pain [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Disease progression [A] *	0/100 (0%)	1/99 (1.01%)	2/102 (1.96%)
General physical health deterioration [A] *	1/100 (1%)	1/99 (1.01%)	0/102 (0%)
Mucosal inflammation [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Pyrexia [A] *	3/100 (3%)	1/99 (1.01%)	1/102 (0.98%)
Sudden death [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Hepatobiliary disorders			
Jaundice cholestatic [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Infections and infestations			
Central line infection [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Infection [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Septic shock [A] *	2/100 (2%)	0/99 (0%)	0/102 (0%)
Tuberculosis [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Injury, poisoning and procedural complications			

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Device migration [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Wound dehiscence [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Metabolism and nutrition disorders			
Anorexia [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Dehydration [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Musculoskeletal and connective tissue disorders			
Back pain [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung squamous cell carcinoma stage unspecified [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Nervous system disorders			
Cerebral ischaemia [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Dizziness [A] *	2/100 (2%)	0/99 (0%)	0/102 (0%)
Spinal cord compression [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Syncope [A] *	1/100 (1%)	1/99 (1.01%)	0/102 (0%)
Renal and urinary disorders			
Calculus urinary [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Hydronephrosis [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Nephrotic syndrome [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Renal failure [A] *	1/100 (1%)	0/99 (0%)	1/102 (0.98%)
Renal vein thrombosis [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Respiratory, thoracic and mediastinal disorders			
Pharyngeal oedema [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Pneumonitis [A] *	1/100 (1%)	1/99 (1.01%)	0/102 (0%)
Productive cough [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Pulmonary artery thrombosis [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Pulmonary embolism [A] *	2/100 (2%)	2/99 (2.02%)	0/102 (0%)
Pulmonary microemboll [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Respiratory failure [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Surgical and medical procedures			
Toe amputation [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Vascular disorders			
Deep vein thrombosis [A] *	2/100 (2%)	3/99 (3.03%)	0/102 (0%)
Embolism [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Hypertension [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)

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

Other Adverse Events

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

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	95/100 (95%)	88/99 (88.89%)	85/102 (83.33%)
Blood and lymphatic system disorders			
Anaemia [A] *	18/100 (18%)	7/99 (7.07%)	6/102 (5.88%)
Febrile neutropenia [A] *	3/100 (3%)	1/99 (1.01%)	0/102 (0%)
Granulocytopenia [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Leukocytosis [A] *	1/100 (1%)	1/99 (1.01%)	1/102 (0.98%)
Leukopenia [A] *	7/100 (7%)	2/99 (2.02%)	2/102 (1.96%)
Neutropenia [A] *	33/100 (33%)	5/99 (5.05%)	6/102 (5.88%)
Pancytopenia [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Thrombocytopenia [A] *	5/100 (5%)	1/99 (1.01%)	2/102 (1.96%)
Cardiac disorders			
Arrhythmia [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Atrial tachycardia [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Bradycardia [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Cyanosis [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Extrasystoles [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Palpitations [A] *	0/100 (0%)	2/99 (2.02%)	1/102 (0.98%)
Sinus tachycardia [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Tachycardia [A] *	0/100 (0%)	2/99 (2.02%)	1/102 (0.98%)
Ventricular extrasystoles [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Ear and labyrinth disorders			
Ear pain [A] *	0/100 (0%)	1/99 (1.01%)	1/102 (0.98%)
Vertigo [A] *	1/100 (1%)	2/99 (2.02%)	3/102 (2.94%)
Endocrine disorders			
Hypothyroidism [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Eye disorders			
Conjunctival haemorrhage [A] *	2/100 (2%)	0/99 (0%)	0/102 (0%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Conjunctivitis [A] *	1/100 (1%)	6/99 (6.06%)	2/102 (1.96%)
Diplopia [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Eye inflammation [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Glaucoma [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Ocular discomfort [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Ocular icterus [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Vision blurred [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Gastrointestinal disorders			
Abdominal discomfort [A] *	1/100 (1%)	0/99 (0%)	1/102 (0.98%)
Abdominal pain [A] *	21/100 (21%)	11/99 (11.11%)	21/102 (20.59%)
Abdominal pain upper [A] *	13/100 (13%)	8/99 (8.08%)	8/102 (7.84%)
Anal discomfort [A] *	1/100 (1%)	0/99 (0%)	1/102 (0.98%)
Ano-rectal ulcer [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Ascites [A] *	0/100 (0%)	1/99 (1.01%)	1/102 (0.98%)
Cheilitis [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Constipation [A] *	12/100 (12%)	10/99 (10.1%)	8/102 (7.84%)
Diarrhoea [A] *	56/100 (56%)	34/99 (34.34%)	28/102 (27.45%)
Dry mouth [A] *	2/100 (2%)	0/99 (0%)	0/102 (0%)
Dyspepsia [A] *	4/100 (4%)	3/99 (3.03%)	4/102 (3.92%)
Enteritis [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Flatulence [A] *	2/100 (2%)	0/99 (0%)	0/102 (0%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Gastritis [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Gastrooesophageal reflux disease [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Gingival bleeding [A] *	0/100 (0%)	2/99 (2.02%)	0/102 (0%)
Gingivitis [A] *	1/100 (1%)	0/99 (0%)	1/102 (0.98%)
Haematochezia [A] *	3/100 (3%)	1/99 (1.01%)	1/102 (0.98%)
Haemorrhoids [A] *	3/100 (3%)	2/99 (2.02%)	2/102 (1.96%)
Intestinal obstruction [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Mesenteric vein thrombosis [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Mouth haemorrhage [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Mouth ulceration [A] *	0/100 (0%)	3/99 (3.03%)	0/102 (0%)
Nausea [A] *	35/100 (35%)	16/99 (16.16%)	26/102 (25.49%)
Oedema peripheral [A] *	2/100 (2%)	1/99 (1.01%)	1/102 (0.98%)
Oral discomfort [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Periodontitis [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Polyp colorectal [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Proctalgia [A] *	0/100 (0%)	1/99 (1.01%)	2/102 (1.96%)
Proctitis [A] *	2/100 (2%)	1/99 (1.01%)	1/102 (0.98%)
Rectal haemorrhage [A] *	1/100 (1%)	2/99 (2.02%)	2/102 (1.96%)
Stomatitis [A] *	6/100 (6%)	10/99 (10.1%)	2/102 (1.96%)
Toothache [A] *	1/100 (1%)	0/99 (0%)	2/102 (1.96%)
Vomiting [A] *	23/100 (23%)	13/99 (13.13%)	6/102 (5.88%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
General disorders			
Asthenia [A] *	16/100 (16%)	17/99 (17.17%)	20/102 (19.61%)
Catheter site related reaction [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Chest discomfort [A] *	0/100 (0%)	1/99 (1.01%)	1/102 (0.98%)
Chest pain [A] *	1/100 (1%)	3/99 (3.03%)	4/102 (3.92%)
Facial pain [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Fatigue [A] *	14/100 (14%)	12/99 (12.12%)	16/102 (15.69%)
General physical health deterioration [A] *	1/100 (1%)	1/99 (1.01%)	2/102 (1.96%)
Influenza-like illness [A] *	1/100 (1%)	3/99 (3.03%)	1/102 (0.98%)
Local swelling [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Malaise [A] *	0/100 (0%)	1/99 (1.01%)	1/102 (0.98%)
Mucosal inflammation [A] *	13/100 (13%)	9/99 (9.09%)	7/102 (6.86%)
Oedema peripheral [A] *	2/100 (2%)	1/99 (1.01%)	1/102 (0.98%)
Pain [A] *	0/100 (0%)	2/99 (2.02%)	1/102 (0.98%)
Pyrexia [A] *	30/100 (30%)	17/99 (17.17%)	15/102 (14.71%)
Hepatobiliary disorders			
Hepatic failure [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Hepatic pain [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Hepatotoxicity [A] *	1/100 (1%)	0/99 (0%)	1/102 (0.98%)
Hyperbilirubinaemia [A] *	10/100 (10%)	22/99 (22.22%)	26/102 (25.49%)
Jaundice [A] *	3/100 (3%)	0/99 (0%)	2/102 (1.96%)
Infections and infestations			

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Abdominal wall infection [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Bacteriuria [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Bronchitis [A] *	0/100 (0%)	2/99 (2.02%)	2/102 (1.96%)
Cellulitis [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Cystitis [A] *	1/100 (1%)	4/99 (4.04%)	1/102 (0.98%)
Dental caries [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Ear infection [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Erysipelas [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Folliculitis [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Gastroenteritis viral [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Herpes zoster [A] *	2/100 (2%)	0/99 (0%)	1/102 (0.98%)
Influenza [A] *	3/100 (3%)	4/99 (4.04%)	5/102 (4.9%)
Nail infection [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Paronychia [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Perianal abscess [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Pharyngitis [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Relapsing fever [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Rhinitis [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Subcutaneous abscess [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Tooth abscess [A] *	3/100 (3%)	1/99 (1.01%)	2/102 (1.96%)
Urinary tract infection [A] *	0/100 (0%)	0/99 (0%)	3/102 (2.94%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Vaginal infection [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Injury, poisoning and procedural complications			
Intestinal stoma complication [A] *	1/100 (1%)	1/99 (1.01%)	1/102 (0.98%)
Radius fracture [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Wound [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Wound dehiscence [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Investigations			
Alanine aminotransferase increased [A] *	7/100 (7%)	9/99 (9.09%)	12/102 (11.76%)
Aspartate aminotransferase increased [A] *	6/100 (6%)	8/99 (8.08%)	11/102 (10.78%)
Blood alkaline phosphatase [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Blood alkaline phosphatase increased [A] *	6/100 (6%)	4/99 (4.04%)	4/102 (3.92%)
Blood bilirubin [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Blood calcium decreased [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Blood calcium increased [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Blood creatine increased [A] *	1/100 (1%)	1/99 (1.01%)	0/102 (0%)
Blood creatinine increased [A] *	1/100 (1%)	4/99 (4.04%)	2/102 (1.96%)
Blood glucose increased [A] *	2/100 (2%)	1/99 (1.01%)	1/102 (0.98%)
Blood lactate dehydrogenase increased [A] *	2/100 (2%)	2/99 (2.02%)	1/102 (0.98%)
Blood sodium increased [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Coagulation test abnormal [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Gamma-glutamyltransferase increased [A] *	0/100 (0%)	1/99 (1.01%)	1/102 (0.98%)
Haematocrit decreased [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Hepatic enzyme increased [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Platelet count increased [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Prothrombin time shortened [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Transaminases increased [A] *	0/100 (0%)	3/99 (3.03%)	0/102 (0%)
Weight decreased [A] *	1/100 (1%)	0/99 (0%)	2/102 (1.96%)
Metabolism and nutrition disorders			
Anorexia [A] *	9/100 (9%)	5/99 (5.05%)	5/102 (4.9%)
Dehydration [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Diabetes mellitus [A] *	0/100 (0%)	1/99 (1.01%)	1/102 (0.98%)
Gout [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Hypercalcaemia [A] *	0/100 (0%)	1/99 (1.01%)	1/102 (0.98%)
Hyperglycaemia [A] *	2/100 (2%)	1/99 (1.01%)	0/102 (0%)
Hyperkalaemia [A] *	2/100 (2%)	0/99 (0%)	1/102 (0.98%)
Hypertriglyceridaemia [A] *	0/100 (0%)	1/99 (1.01%)	1/102 (0.98%)
Hyperuricaemia [A] *	2/100 (2%)	1/99 (1.01%)	3/102 (2.94%)
Hypoalbuminaemia [A] *	1/100 (1%)	0/99 (0%)	2/102 (1.96%)
Hypocalcaemia [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Hypokalaemia [A] *	3/100 (3%)	1/99 (1.01%)	2/102 (1.96%)
Musculoskeletal and connective tissue disorders			
Arthralgia [A] *	5/100 (5%)	4/99 (4.04%)	4/102 (3.92%)
Arthritis [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Back pain [A] *	5/100 (5%)	2/99 (2.02%)	4/102 (3.92%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Bone pain [A] *	3/100 (3%)	0/99 (0%)	1/102 (0.98%)
Buttock pain [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Chest wall pain [A] *	0/100 (0%)	2/99 (2.02%)	1/102 (0.98%)
Muscle spasms [A] *	0/100 (0%)	0/99 (0%)	2/102 (1.96%)
Musculoskeletal pain [A] *	1/100 (1%)	1/99 (1.01%)	0/102 (0%)
Myalgia [A] *	1/100 (1%)	2/99 (2.02%)	1/102 (0.98%)
Neck pain [A] *	0/100 (0%)	2/99 (2.02%)	3/102 (2.94%)
Pain in extremity [A] *	2/100 (2%)	2/99 (2.02%)	5/102 (4.9%)
Periarthritis [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Sacral pain [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Shoulder pain [A] *	3/100 (3%)	2/99 (2.02%)	2/102 (1.96%)
Tendonitis [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Nervous system disorders			
Carpal tunnel syndrome [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Cholinergic syndrome [A] *	5/100 (5%)	0/99 (0%)	0/102 (0%)
Coordination abnormal [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Dizziness [A] *	3/100 (3%)	0/99 (0%)	1/102 (0.98%)
Dysaesthesia [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Dysguesia [A] *	1/100 (1%)	0/99 (0%)	1/102 (0.98%)
Headache [A] *	4/100 (4%)	7/99 (7.07%)	5/102 (4.9%)
Migraine without aura [A] *	2/100 (2%)	0/99 (0%)	0/102 (0%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Neuropathy [A] *	3/100 (3%)	0/99 (0%)	1/102 (0.98%)
Paraesthesia [A] *	4/100 (4%)	3/99 (3.03%)	5/102 (4.9%)
Sciatica [A] *	1/100 (1%)	3/99 (3.03%)	2/102 (1.96%)
Somnolence [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Syncope [A] *	2/100 (2%)	0/99 (0%)	0/102 (0%)
Psychiatric disorders			
Anxiety [A] *	0/100 (0%)	3/99 (3.03%)	1/102 (0.98%)
Confusional state [A] *	1/100 (1%)	0/99 (0%)	1/102 (0.98%)
Depression [A] *	1/100 (1%)	1/99 (1.01%)	3/102 (2.94%)
Insomnia [A] *	2/100 (2%)	2/99 (2.02%)	1/102 (0.98%)
Mood altered [A] *	0/100 (0%)	1/99 (1.01%)	1/102 (0.98%)
Panic attack [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Restlessness [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Renal and urinary disorders			
Bladder spasm [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Dysuria [A] *	2/100 (2%)	0/99 (0%)	0/102 (0%)
Nocturia [A] *	1/100 (1%)	0/99 (0%)	1/102 (0.98%)
Pollakiuria [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Proteinuria [A] *	4/100 (4%)	4/99 (4.04%)	4/102 (3.92%)
Renal colic [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Renal failure acute [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Ureteric obstruction [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Ureteric stenosis [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Reproductive system and breast disorders			
Female genital-digestive tract fistula [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Pelvic pain [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Penis disorder [A] *	0/100 (0%)	3/99 (3.03%)	1/102 (0.98%)
Rhinorrhoea [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Vaginal haemorrhage [A] *	0/100 (0%)	0/99 (0%)	2/102 (1.96%)
Respiratory, thoracic and mediastinal disorders			
Cough [A] *	5/100 (5%)	3/99 (3.03%)	6/102 (5.88%)
Dysphonia [A] *	1/100 (1%)	0/99 (0%)	2/102 (1.96%)
Dyspnoea [A] *	4/100 (4%)	5/99 (5.05%)	6/102 (5.88%)
Epistaxis [A] *	14/100 (14%)	6/99 (6.06%)	7/102 (6.86%)
Haemoptysis [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Pharyngolaryngeal pain [A] *	4/100 (4%)	3/99 (3.03%)	1/102 (0.98%)
Pleural effusion [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Productive cough [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Sleep apnoea syndrome [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Skin and subcutaneous tissue disorders			
Alopecia [A] *	22/100 (22%)	2/99 (2.02%)	3/102 (2.94%)
Dry skin [A] *	0/100 (0%)	2/99 (2.02%)	0/102 (0%)
Erythema [A] *	5/100 (5%)	0/99 (0%)	1/102 (0.98%)
Erythema [A] *	5/100 (5%)	0/99 (0%)	1/102 (0.98%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Hyperhidrosis [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Nail disorder [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Nail dystrophy [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Onycholysis [A] *	0/100 (0%)	2/99 (2.02%)	0/102 (0%)
Palmar-plantar erythrodysaesthesia syndrome [A] *	16/100 (16%)	40/99 (40.4%)	39/102 (38.24%)
Photosensitivity reaction [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Pruritus [A] *	0/100 (0%)	1/99 (1.01%)	2/102 (1.96%)
Rash [A] *	3/100 (3%)	1/99 (1.01%)	3/102 (2.94%)
Rash papular [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Skin exfoliation [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Skin fissures [A] *	0/100 (0%)	2/99 (2.02%)	0/102 (0%)
Urticaria [A] *	1/100 (1%)	1/99 (1.01%)	0/102 (0%)
Surgical and medical procedures			
Cataract operation [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Inguinal hernia repair [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Stent placement [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Tooth extraction [A] *	0/100 (0%)	1/99 (1.01%)	0/102 (0%)
Vascular disorders			
Axillary vein thrombosis [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)
Deep vein thrombosis [A] *	3/100 (3%)	1/99 (1.01%)	1/102 (0.98%)
Haemorrhage [A] *	0/100 (0%)	0/99 (0%)	1/102 (0.98%)

	Bevacizumab + Irinotecan + Capecitabine (1000 mg/m^2)	Bevacizumab + Capecitabine (1250 mg/m^2)	Bevacizumab + Capecitabine (650 mg/m^2)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Hypertension [A] *	28/100 (28%)	29/99 (29.29%)	19/102 (18.63%)
Hypotension [A] *	1/100 (1%)	1/99 (1.01%)	0/102 (0%)
Phlebitis [A] *	1/100 (1%)	0/99 (0%)	0/102 (0%)
Thrombosis [A] *	2/100 (2%)	0/99 (0%)	1/102 (0.98%)

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

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

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

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

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