ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 08/05/2015

ClinicalTrials.gov ID: NCT00528567

Study Identification

Unique Protocol ID:	BO20289
Brief Title:	BEATRICE Study: A Study of Bevacizumab (Avastin) Adjuvant Therapy in Triple Negative Breast Cancer
Official Title:	An International Multi-centre Open-label 2-arm Phase III Trial of Adjuvant Bevacizumab in "Triple Negative" Breast Cancer.
Secondary IDs:	2007-001128-11 [EudraCT Number]

Study Status

Record Verification:	August 2015
Overall Status:	Completed
Study Start:	December 2007
Primary Completion:	February 2012 [Actual]
Study Completion:	June 2014 [Actual]

Sponsor/Collaborators

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

Oversight

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

Review Board:	Approval Status: Approved Approval Number: PC/AP 21-2007 Board Name: Comite de protection des personnes ile de France X Board Affiliation: Hopital Robert Ballanger Phone: 0033 01 49 36 73 57 Email: cpp.iledefrance10@ch-aulnay.fr
Data Monitoring?:	
Plan to Share Data?:	
Oversight Authorities:	France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)

Study Description

Brief Summary: The main objective of the trial is to compare Invasive Disease-Free Survival (IDFS) of patients randomised to treatment with adjuvant chemotherapy alone or to adjuvant chemotherapy with 1 year of bevacizumab.

The secondary objectives of this trial are to:

- compare Overall Survival (OS), Breast Cancer-Free Interval (BCFI), Disease- Free Survival (DFS) and Distant Disease-Free Survival (DDFS) of patients randomised to treatment with adjuvant chemotherapy alone or to adjuvant chemotherapy in combination with 1 year of bevacizumab
- evaluate the safety and tolerability of bevacizumab

An exploratory sub-study (not reported here) was to identify biomarkers (from tumour or serum) predictive of toxicity and for the level of benefit from the addition of bevacizumab to standard adjuvant systemic treatment.

Detailed Description:

Conditions

Conditions:	Breast Cancer
Keywords:	

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment
Study Phase:	Phase 3
Intervention Model:	Parallel Assignment
Number of Arms:	2

Masking:	Open Label
Allocation:	Randomized
Endpoint Classification:	Safety/Efficacy Study
Enrollment:	2591 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Bevacizumab and Chemotherapy Participants randomized to receive bevacizumab in combination with chemotherapy as prescribed.	Drug: Bevacizumab Bevacizumab was administered at a dose equivalent of 5 mg/kg/week using 1 of 3 different scheduling options depending on the schedule of the adjuvant chemotherapy regimen selected for an individual patient. Other Names: • Avastin Drug: Standard adjuvant chemotherapy All chemotherapy schedules and doses for each patient were prescribed according to the labeled indication of the country in which the patient was receiving therapy.
Active Comparator: Chemotherapy Participants randomized to receive standard adjuvant chemotherapy as prescribed.	Drug: Standard adjuvant chemotherapy All chemotherapy schedules and doses for each patient were prescribed according to the labeled indication of the country in which the patient was receiving therapy.

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Gender:	Both
Accepts Healthy Volunteers?:	No
Criteria:	Inclusion Criteria:

- adult patients, >=18 years of age;
- operable primary invasive breast cancer;
- completed definitive loco-regional surgery;

- primary tumor centrally confirmed as triple negative.

Exclusion Criteria:

- locally advanced breast cancers;
- previous breast cancer history;
- clinically significant cardiovascular disease.

Contacts/Locations

Study Officials: Clinical Trials
Study Director
Hoffmann-La Roche

Locations: Canada, Alberta
Edmonton, Alberta, Canada, T6G 1Z2

Canada, Ontario
Oshawa, Ontario, Canada, L1G 2B9

Canada, Manitoba
Winnipeg, Manitoba, Canada, R2H 2A6

Canada, Quebec
Montreal, Quebec, Canada, H1T 2M4

Canada, Ontario
Windsor, Ontario, Canada, N8W 2X3

Canada, Newfoundland and Labrador
St. John's, Newfoundland and Labrador, Canada, A1B 3V6

Canada, Quebec
Greenfield Park, Quebec, Canada, J4V 2H1

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

Canada, Ontario
Kingston, Ontario, Canada, K7L 5P9

Canada, British Columbia
Surrey, British Columbia, Canada, V3V 1Z2

Canada, Quebec

Montreal, Quebec, Canada, H2W 1S6

Quebec, Quebec, Canada, G1S 4L8

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

Canada, Saskatchewan
Saskatoon, Saskatchewan, Canada, S7N 4H4

Canada, Ontario
Toronto, Ontario, Canada, M5G 2M9

London, Ontario, Canada, N6A 4L6

Toronto, Ontario, Canada, M9N 1N8

Sudbury, Ontario, Canada, P3E 5J1

Austria
Salzburg, Austria, 5020

Leoben, Austria, 8700

Wien, Austria, 1090

Wiener Neustadt, Austria, 2700

Bludesch, Austria, 6712

Innsbruck, Austria, 6020

Wolfsberg, Austria, 9400

Graz, Austria, 8036

Wien, Austria, 1130

Wien, Austria, 1090

Wels, Austria, 4600

France
Angers, France, 49933

Colmar, France, 68024

Tours, France, 37044

Saint-cloud, France, 92210

Toulon, France, 83056

Senlis, France, 60309

Grenoble, France, 38100

Strasbourg, France, 67010

Paris, France, 75908

La Chaussee St Victor, France, 41260

Paris, France, 75010

Montbeliard, France, 25209

Bobigny, France, 93009

Besancon, France, 25030

Montpellier, France, 34298

Bayonne, France, 64100

Nancy, France, 54100

Lille, France, 59020

Neuilly Sur Seine, France, 92200

Rouen, France, 76038

Singapore

Singapore, Singapore, 119228

Australia

Camperdown, Australia, 2050

Geelong, Australia, 3220

Sydney, Australia, 2060

Perth, Australia, 6000

Wahroonga, Australia, 2076

Fitzroy, Australia, 3065

Waratah, Australia, 2298

Sydney, Australia, 2065

Port Macquarie, Australia, 2444

Wollongong, Australia, 2500

Nambour, Australia, 4560

Parkville, Australia, 3052

Perth, Australia, 6008

Kurralta Park, Australia, 5035

Brisbane, Australia, 4104

Heidelberg, Australia, 3084

East Bentleigh, Australia, VIC 3165

Canada, New Brunswick

Moncton, New Brunswick, Canada, E1C 6Z8

Singapore

Singapore, Singapore, 169610

Australia

Brisbane, Australia, 4006

Malvern, Australia, 3144

Sydney, Australia, 2139

France

Le Mans, France, 72000

Marseille, France, 13285

Bordeaux, France, 33077

Paris, France, 75231

Clermont Ferrand, France, 63050

Limoges, France, 87039

Mougins, France, 6250

Lille, France, 59000

Canada, Ontario
Ottawa, Ontario, Canada, K1H 8L6

Argentina
Buenos Aires, Argentina, C1405DCS

Rosario, Argentina, S2002KDS

Bosnia and Herzegovina
Sarajevo, Bosnia and Herzegovina, 71000

Czech Republic
Brno, Czech Republic, 656 53

Praha, Czech Republic, 150 06

Olomouc, Czech Republic, 775 20

Novy Jicin, Czech Republic, 741 01

Pardubice, Czech Republic, 532 03

Finland
Tampere, Finland, 33520

Belgium
Wilrijk, Belgium, 2610

Baudour, Belgium, 7331

Hasselt, Belgium, 3500

Bruxelles, Belgium, 1090

Brazil
Porto Alegre, Brazil, 91350-200

Sao Paulo, Brazil, 01209-010

Rio de Janeiro, Brazil, 22260-020

Sao Paulo, Brazil, 1401000

Porto Alegre, Brazil, 90035-903

Santo Andre, Brazil, 09060-870

Sao Paulo, Brazil, 05403

JAU, Brazil, 17210-120

China

Beijing, China, 100021

Beijing, China, 100071

Shanghai, China, 200032

Wuhan, China, 430030

Suzhou, China, 215006

Hang Zhou, China, 310022

Zhejiang, China, 310003

Costa Rica

San Jose, Costa Rica, 10103

Germany

Georgsmarienhütte, Germany, 49124

WEIßENFELS, Germany, 06667

Herne, Germany, 44625

Lemgo, Germany, 32657

ULM, Germany, 89075

Berlin, Germany, 14195

Heidelberg, Germany, 69115

Greifswald, Germany, 17475

Dresden, Germany, 01307

Kassel, Germany, 34117

Berlin, Germany, 10317

Recklinghausen, Germany, 45657

Kiel, Germany, 24105

Witten, Germany, 58452

Tübingen, Germany, 72076

Hamburg, Germany, 20357

Krefeld, Germany, 47805

Trier, Germany, 54290

Freiburg, Germany, 79106

Koeln, Germany, 50924

Magdeburg, Germany, 39108

Leipzig, Germany, 04129

Hamburg, Germany, 20246

Frankfurt Am Main, Germany, 60389

Greece

Thessaloniki, Greece, 56429

Heraklion, Greece, 71110

Patras, Greece, 26500

Hong Kong

Hong Kong, Hong Kong, 852

Hong Kong, Hong Kong

Israel

Haifa, Israel, 31096

Ramat-gan, Israel, 52621

Tel Aviv, Israel, 64239

Italy

Vecchiazzano, Italy, 47100

Lido Di Camaiore, Italy, 55043

Noale, Italy, 30033

Treviglio, Italy, 24047

Pavia, Italy, 27100

Brindisi, Italy, 72100

Bari, Italy, 70126

Sassari, Italy, 07100

Roma, Italy, 00161

Lugo, Italy

Livorno, Italy, 57100

Taormina, Italy, 98039

Palermo, Italy, 90146

Lecce, Italy, 73100

San Giovanni Rotondo, Italy, 71013

Potenza, Italy, 85100

Ravenna, Italy, 48100

Fano, Italy, 61032

Candiolo, Italy, 10060

Roma, Italy, 00158

Cattolica, Italy, 47841

Pavia, Italy, 27100

Rimini, Italy, 47037

Parma, Italy, 43100

Rozzano, Italy, 20089

Brescia, Italy, 25123

Bergamo, Italy, 24128

Aviano, Italy, 33081

Pavia, Italy, 27100

Genova, Italy, 16142

Korea, Republic of
Seoul, Korea, Republic of, 138-736

Seoul, Korea, Republic of, 135-170

Seoul, Korea, Republic of, 110-744

Kyunggi-do, Korea, Republic of, 411-769

Seoul, Korea, Republic of, 137-702

Macedonia, The Former Yugoslav Republic of
Skopje, Macedonia, The Former Yugoslav Republic of, 1000

Mexico
Leon, Mexico, 37000

Monterrey, Mexico, 64020

New Zealand
Auckland, New Zealand

Wellington, New Zealand, 6002

Peru
Lima, Peru, 11

Philippines
Quezon City, Philippines, 1114

Cebu, Philippines, 6000

Poland
Lublin, Poland, 20-090

Lodz, Poland, 93-509

Warsaw, Poland, 61485

Lublin, Poland, 20-081

Elblag, Poland, 82-300

Poznan, Poland, 61-878

Warszawa, Poland, 02-781

Portugal
Coimbra, Portugal, 3000-075

Lisboa, Portugal, 1099-023

Lisboa, Portugal, 1649-035

Romania
Bucharest, Romania, 022328

Cluj Napoca, Romania, 400015

Russian Federation
Kazan, Russian Federation, 420111

Chelyabinsk, Russian Federation, 454 087

Ivanovo, Russian Federation, 153040

Ekaterinburg, Russian Federation, 620905

Moscow, Russian Federation, 121356

St Petersburg, Russian Federation

Moscow, Russian Federation, 117837

Kazan, Russian Federation, 420029

Samara, Russian Federation, 443066

Ryazan, Russian Federation, 390011

UFA, Russian Federation, 450054

Persochnysaint-petersburg, Russian Federation, 197758

Obninsk, Russian Federation, 249036

Serbia

Sremska Kamenica, Serbia, 21204

Belgrade, Serbia, 11000

South Africa

Pretoria, South Africa, 0181

Pretoria, South Africa, 0002

Johannesburg, South Africa, 2196

Pietermaritzburg, South Africa, 3201

Bloemfontein, South Africa, 9301

Durban, South Africa, 4001

Spain

Málaga, Spain, 29010

Barcelona, Spain, 08003

La Laguna, Spain, 38320

Malaga, Spain, 29010

Madrid, Spain, 28041

Pontevedra, Spain, 36002

Madrid, Spain, 28222

Navarra, Spain, 31008

Madrid, Spain, 28046

Valencia, Spain, 41014

Barcelona, Spain, 08035

Madrid, Spain, 28034

Madrid, Spain, 28033

Mataro, Spain, 08304

Zaragoza, Spain, 50009

Valencia, Spain, 46017

Gijon, Spain, 33394

Palma de Mallorca, Spain, 07014

Girona, Spain, 17007

Sweden

Umea, Sweden, 90185

Uppsala, Sweden, 751 85

Gaevle, Sweden, 80187

Lund, Sweden, 22185

Malmoe, Sweden, 20502

Switzerland

Thun, Switzerland, 3600

Basel, Switzerland, 4031

Bern, Switzerland, 3010

Chur, Switzerland, 7000

Taiwan

Kaohsiung, Taiwan, 807

Taipei, Taiwan, 112

Tainan, Taiwan, 704

Taipei, Taiwan, 114

Taipei, Taiwan, 100

Changhua, Taiwan, 500

Kaohsiung, Taiwan, 813

Taoyuan, Taiwan, 333

Thailand

Bangkok, Thailand, 10400

Chiang Mai, Thailand, 50200

Bangkok, Thailand, 10700

Bangkok, Thailand, 10400

Songkhla, Thailand, 90110

United Kingdom

Cardiff, United Kingdom, CF14 2TL

Brighton, United Kingdom, BN2 5BE

Newcastle Upon Tyne, United Kingdom, NE4 6BE

Bristol, United Kingdom, BS2 8ED

Stoke-on-trent, United Kingdom, ST4 7LN

Leeds, United Kingdom, LS9 7TF

Glasgow, United Kingdom, G12 0YN

London, United Kingdom, SE1 9RT

Bournemouth, United Kingdom, BH7 7DW

Exeter, United Kingdom, EX2 5DW

Guildford, United Kingdom, GU2 5XX

Huddersfield, United Kingdom, HD3 3EA

London, United Kingdom, NW3 2QG

Belfast, United Kingdom, BT9 7AB

Northwood, United Kingdom, HA6 2RN

Merseyside, United Kingdom, CH63 45Y

Birmingham, United Kingdom, B15 2TT

Epping, United Kingdom, CM16 6TN

Dundee, United Kingdom, DD1 9SY

Manchester, United Kingdom, M20 4BX

Truro, United Kingdom, TR1 3LJ

Cambridge, United Kingdom, CB2 2QQ

Edinburgh, United Kingdom, EH4 2XU

Colchester, United Kingdom, CO3 3NB

Malaysia
Penang, Malaysia, 11200

Petaling Jaya, Selangor, Malaysia, 46050

Kelantan, Malaysia

Netherlands
Groningen, Netherlands, 9713 GZ

Den Helder, Netherlands, 1782GZ

France
Brest, France, 29609

Hong Kong
Hong Kong, Hong Kong, 852

United States, District of Columbia
Washington, District of Columbia, United States, 20010

United States, Florida
Gainesville, Florida, United States, 32605

United States, Georgia
Augusta, Georgia, United States, 30901

United States, North Carolina
Hickory, North Carolina, United States, 28602

United States, Maryland
Baltimore, Maryland, United States, 21237

United States, California
Bakersfield, California, United States, 93309

United States, Florida
Tamarac, Florida, United States, 33321

United States, Virginia
Abingdon, Virginia, United States, 24211

United States, California
Greenbrae, California, United States, 94904

Malaysia
Selangor, Malaysia, 47500

Netherlands
Tilburg, Netherlands, 5042 AD

Philippines
Quezon City, Philippines, 1114

Romania
Bucharest, Romania, 022328

United States, Vermont
Rutland, Vermont, United States, 05701

United States, Texas
Austin, Texas, United States, 78759

United States, Maryland
Baltimore, Maryland, United States, 21215

Canada, Ontario
Toronto, Ontario, Canada, M4N 3M5

United States, Michigan
Southfield, Michigan, United States, 48075-3707

Kalamazoo, Michigan, United States, 49007

United States, Missouri
St Louis, Missouri, United States, 63141

United States, Tennessee
Nashville, Tennessee, United States, 37203

United States, Connecticut
Fairfield, Connecticut, United States, 06824

United States, Florida
Orlando, Florida, United States, 32806

Spain
Burgos, Spain, 09005

United States, Iowa
Waterloo, Iowa, United States, 50702

United States, Ohio
Middletown, Ohio, United States, 45042

United States, Maryland
Rockville, Maryland, United States, 20850-3348

United States, Connecticut
Stamford, Connecticut, United States, 06902

United States, Georgia
Lawrenceville, Georgia, United States, 30046

Atlanta, Georgia, United States, 30318

United States, California
Fountain Valley, California, United States, 92708

Los Angeles, California, United States, 90057

Pleasant Hill, California, United States, 94523

United States, South Carolina
Columbia, South Carolina, United States, 29210

United States, New Jersey
Long Branch, New Jersey, United States, 07740

United States, Illinois

Niles, Illinois, United States, 60714

United States, Michigan
Brownstown, Michigan, United States, 48183

United States, Missouri
Kansas City, Missouri, United States, 64111

United States, Arkansas
Fayetteville, Arkansas, United States, 72703

United States, Tennessee
Germantown, Tennessee, United States, 38138

United States, Ohio
Columbus, Ohio, United States, 43235

United States, Alabama
Mobile, Alabama, United States, 36604

Italy
Roma, Italy, 00144

Finland
Turku, Finland, 20521

Brazil
Porto Alegre, Brazil, 90430-090

Netherlands
Delftzijl, Netherlands, 9934 JD

Japan
Tokyo, Japan, 135-8550

Tokyo, Japan, 104-0045

Aichi, Japan, 464-8681

Tokyo, Japan, 104-8560

Saitama, Japan, 350-1298

Kyoto, Japan, 606-8507

Osaka, Japan, 540-0006

Ehime, Japan, 791-0280

Fukuoka, Japan, 811-1395

Russian Federation
Moscow, Russian Federation, 115478

Belgium
Sint-niklaas, Belgium, 9100

Italy
Cesena, Italy, 47023

Japan
Tokyo, Japan, 113-8677

Spain
Terrassa, Spain, 08221

Australia
Sydney, Australia, 2031

Wodonga, Australia, 3690

Germany
Rosenheim, Germany, 83022

Australia
St. Leonards, Australia, 2065

Israel
Rehovot, Israel, 76100

Kfar Saba, Israel, 44281

Petach Tikva, Israel, 49100

Jerusalem, Israel, 91120

Switzerland
Zürich, Switzerland, 8008

Aarau, Switzerland, 5001

Winterthur, Switzerland, 8401

United Kingdom

Southampton, United Kingdom, SO16 6YD

Sheffield, United Kingdom, S1O 2SJ

Wolverhampton, United Kingdom, WV10 0QP

Peterborough, United Kingdom, PE 3 9GZ

Italy
Padova, Italy, 35128

Hong Kong
Hong Kong, Hong Kong

Hong Kong, Hong Kong

Brazil
Sorocaba, Brazil, 18030-245

Ijui, Brazil, 98700-000

Goiania, Brazil, 74075-040

Sao Paulo, Brazil, 01317-000

Germany
Bielefeld, Germany, 33604

Münster, Germany, 48149

Coburg, Germany, 96450

Offenbach, Germany, 63069

Dortmund, Germany, 44137

Chemnitz, Germany, 09116

Marburg, Germany, 35043

Stade, Germany, 21680

München, Germany, 81925

United Kingdom
London, United Kingdom, EC1 A7BE

London, United Kingdom, W2 1NY

United States, New York
Bronx, New York, United States, 10469

United States, Ohio
Cincinnati, Ohio, United States, 45242

United States, Virginia
Richmond, Virginia, United States, 23230

United States, Texas
Dallas, Texas, United States, 75234

United States, Tennessee
Chattanooga, Tennessee, United States, 37404

United States, Iowa
Iowa City, Iowa, United States, 52242

United States, Alabama
Huntsville, Alabama, United States, 35805

Canada, Ontario
Kitchener, Ontario, Canada, N2G 1G3

Italy
Mantova, Italy, 46100

United Kingdom
Chelsmford, United Kingdom, CM1 7ET

Canada, Ontario
Mississauga, Ontario, Canada, L5M 2N1

United States, North Carolina
Winston-salem, North Carolina, United States, 27103

Sweden
Eskilstuna, Sweden, 63188

Germany
Wiesbaden, Germany, 65199

Düsseldorf, Germany, 40225

Bonn, Germany, 53111

Austria
Krems, Austria, 4560

Germany
Offenburg, Germany, 77654

Lüneburg, Germany, 21339

China
Beijing, China, 100853

Tianjin, China, 300060

Belgium
Tournai, Belgium, 7500

United Kingdom
Ipswich, United Kingdom, IP4 5PD

Belgium
Namur, Belgium, 5000

China
Changchun, China, 130012

Guangzhou, China, 510060

Chengdu, China, 610041

Austria
Linz, Austria, 4020

China
Fuzhou, China, 350025

Beijing, China, 100032

References

Citations:

Links:

Study Data/Documents:

Study Results

Participant Flow

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy. For these patients, bevacizumab was given in combination with chemotherapy at a dose of 5 mg/kg/week equivalent using 1 of 3 different scheduling options depending on the schedule of the adjuvant chemotherapy selected. After completing chemotherapy + bevacizumab (treatment period 1), patients in this arm received bevacizumab monotherapy up to a total duration of 1 year (treatment period 2). At the end of treatment (i.e., after approximately 55 weeks), patients were followed up until the end of the study.
Chemotherapy	Participants randomized to receive chemotherapy alone. For patients randomized to the chemotherapy alone arm, investigators could select from one of three chemotherapy regimens. After completing chemotherapy (treatment period 1) patients entered a post-treatment surveillance period for the remainder of the first year after randomization (treatment period 2). At the end of treatment (i.e., after approximately 55 weeks), patients were followed up until the end of the study.

Overall Study

	Bevacizumab and Chemotherapy	Chemotherapy
Started	1301	1290
Intention to Treat	1301	1290
Safety Population	1288	1271
Completed	870	982
Not Completed	431	308
Death	4	5
Breast Cancer Recurrence/2nd Primary	30	60
Adverse Event/Intermittent Illness	255	29
Violation Criteria at Entry	3	17
Withdrew Consent	59	55
Refused Treatment/Did Not Cooperate	52	42

	Bevacizumab and Chemotherapy	Chemotherapy
Failure to Return	1	4
Other Protocol Violation	5	21
Administrative/Other	22	75

Baseline Characteristics

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy alone

Baseline Measures

	Bevacizumab and Chemotherapy	Chemotherapy	Total
Number of Participants	1301	1290	2591
Age, Customized [units: participants]			
< 40 years	231	253	484
>= 40 to < 65 years	952	916	1868
>= 65 years	118	121	239
Gender, Male/Female [units: participants]			
Female	1301	1290	2591
Male	0	0	0

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Time to Invasive Disease-free Survival (IDFS) Event

Measure Description	IDFS, was a composite endpoint defined as the time from randomization until the date of the first occurrence of one of the following events: Ipsilateral invasive breast cancer recurrence (same breast); Ipsilateral (same side of body) local regional invasive breast cancer recurrence (axilla, regional lymph nodes, chest wall, and/or skin); Distant recurrence (evidence of breast cancer in any anatomic site);Death attributable to any cause; Contralateral (opposite side of the body) invasive breast cancer or Second primary non-breast invasive cancer.
Time Frame	Event driven (until data cutoff: 29 February 2012: up to 49 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy alone

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290
Time to Invasive Disease-free Survival (IDFS) Event [units: Months] Median (95% Confidence Interval)	NA (NA to NA) [1]	NA (NA to NA) [1]

[1] The median was not reached.

Statistical Analysis 1 for Time to Invasive Disease-free Survival (IDFS) Event

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

Statistical Test of Hypothesis	P-Value	0.1810
	Comments	[Not specified]
	Method	Log Rank

	Comments	Stratification factors were axillary nodal status, choice of adjuvant chemotherapy, hormone receptor status, surgery.

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.87
	Confidence Interval	(2-Sided) 95% 0.72 to 1.07
	Estimation Comments	[Not specified]

2. Primary Outcome Measure:

Measure Title	Percentage of Participants With Invasive Disease-free Survival (IDFS) Events
Measure Description	IDFS, was a composite endpoint defined as the time from randomization until the date of the first occurrence of one of the following events: Ipsilateral invasive breast cancer recurrence (same breast); Ipsilateral (same side of body) local regional invasive breast cancer recurrence (axilla, regional lymph nodes, chest wall, and/or skin); Distant recurrence (evidence of breast cancer in any anatomic site);Death attributable to any cause; Contralateral (opposite side of the body) invasive breast cancer or Second primary non-breast invasive cancer. The percentage of participants with and without IDFS Events by the time of the data cutoff is presented.
Time Frame	Event driven (until data cutoff: 29 February 2012 up to 49 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy alone

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290
Percentage of Participants With Invasive Disease-free Survival (IDFS) Events [units: Percentage of participants]		
Percentage of Participants with Events	14.5	15.9

	Bevacizumab and Chemotherapy	Chemotherapy
Percentage of Participants without Events	85.5	84.1

3. Primary Outcome Measure:

Measure Title	Time to Invasive Disease-free Survival (IDFS) Event Excluding Second Primary Non-Breast Invasive Cancer
Measure Description	IDFS, was a composite endpoint defined as the time from randomization until the date of the first occurrence of one of the following events: Ipsilateral invasive breast cancer recurrence (same breast); Ipsilateral (same side of body) local regional invasive breast cancer recurrence (axilla, regional lymph nodes, chest wall, and/or skin); Distant recurrence (evidence of breast cancer in any anatomic site); Death attributable to any cause; Contralateral (opposite side of the body) invasive breast cancer.
Time Frame	Event driven (until data cutoff: 29 February 2012: up to 49 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy alone

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290
Time to Invasive Disease-free Survival (IDFS) Event Excluding Second Primary Non-Breast Invasive Cancer [units: Months] Median (95% Confidence Interval)	NA (NA to NA) [1]	NA (NA to NA) [1]

[1] The median was not reached.

Statistical Analysis 1 for Time to Invasive Disease-free Survival (IDFS) Event Excluding Second Primary Non-Breast Invasive Cancer

Statistical Analysis Overview	Comparison Groups	Bevacizumab and Chemotherapy, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1966
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.87
	Confidence Interval	(2-Sided) 95% 0.71 to 1.07
	Estimation Comments	Stratification factors were axillary nodal status, choice of adjuvant chemotherapy, hormone receptor status, surgery.

4. Primary Outcome Measure:

Measure Title	Percentage of Participants With Invasive Disease-free Survival (IDFS) Events Excluding Second Primary Non-Breast Invasive Cancer
Measure Description	IDFS, was a composite endpoint defined as the time from randomization until the date of the first occurrence of one of the following events: Ipsilateral invasive breast cancer recurrence (same breast); Ipsilateral (same side of body) local regional invasive breast cancer recurrence (axilla, regional lymph nodes, chest wall, and/or skin); Distant recurrence (evidence of breast cancer in any anatomic site); Death attributable to any cause; Contralateral (opposite side of the body) invasive breast cancer. Percentage of participants with and without IDFS Events by the time of data cutoff is presented.
Time Frame	Event driven (until data cutoff: 29 February 2012: up to 49 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy alone

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290
Percentage of Participants With Invasive Disease-free Survival (IDFS) Events Excluding Second Primary Non-Breast Invasive Cancer [units: Percentage of participants]		
Percentage of Participants with Events	13.5	14.7
Percentage of Participants without Events	86.5	85.3

5. Secondary Outcome Measure:

Measure Title	Time to Overall Survival (OS) Event
Measure Description	OS was defined as the time from randomization to death attributable to any cause. Patients for whom no death is captured in the clinical database up to the clinical cut-off date are censored at the last time they were known to be alive.
Time Frame	Event driven (until data cutoff: 29 February 2012: up to 49 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290

	Bevacizumab and Chemotherapy	Chemotherapy
Time to Overall Survival (OS) Event [units: Months] Median (95% Confidence Interval)	NA (NA to NA) [1]	NA (NA to NA) [1]

[1] The median was not reached

6. Secondary Outcome Measure:

Measure Title	Time to Overall Survival (OS) Event
Measure Description	OS was defined as the time from randomization to death attributable to any cause. Patients for whom no death is captured in the clinical database up to the clinical cut-off date are censored at the last time they were known to be alive.
Time Frame	Event driven (until data cutoff: 30 June 2014: up to 77 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290
Time to Overall Survival (OS) Event [units: Months] Median (95% Confidence Interval)	NA (NA to NA) [1]	NA (NA to NA) [1]

[1] The median was not estimable.

Statistical Analysis 1 for Time to Overall Survival (OS) Event

Statistical Analysis Overview	Comparison Groups	Bevacizumab and Chemotherapy, Chemotherapy
	Comments	[Not specified]

	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.5247
	Comments	[Not specified]
	Method	Log Rank
	Comments	Stratification factors are Axillary nodal status, Choice of adjuvant chemotherapy, Hormone receptor status, Surgery

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.93
	Confidence Interval	(2-Sided) 95% 0.74 to 1.17
	Estimation Comments	[Not specified]

7. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Overall Survival (OS) Event
Measure Description	OS was defined as the time from randomization to death attributable to any cause. Patients for whom no death is captured in the clinical database up to the clinical cut-off date are censored at the last time they were known to be alive.
Time Frame	Event driven (until data cut off: 29 February 2012: up to 49 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290

	Bevacizumab and Chemotherapy	Chemotherapy
Percentage of Participants With Overall Survival (OS) Event [units: percentage of participants]		
with events	7.1	8.3
without events	92.9	91.7

Statistical Analysis 1 for Percentage of Participants With Overall Survival (OS) Event

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

Statistical Test of Hypothesis	P-Value	0.2318
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.84
	Confidence Interval	(2-Sided) 95% 0.64 to 1.12
	Estimation Comments	[Not specified]

8. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Overall Survival (OS) Event
Measure Description	OS was defined as the time from randomization to death attributable to any cause. Patients for whom no death is captured in the clinical database up to the clinical cut-off date are censored at the last time they were known to be alive.
Time Frame	Event driven (until data cut off: 30 June 2014: up to 77 months)
Safety Issue?	No

Analysis Population Description
Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290
Percentage of Participants With Overall Survival (OS) Event [units: percentage of participants]		
with events	11.1	11.6
without events	88.9	88.4

9. Secondary Outcome Measure:

Measure Title	Time to Breast Cancer-Free Interval (BCFI) Event
Measure Description	BCFI is defined as the time from randomization until the date of the first occurrence of one of the following events: Ipsilateral local/regional invasive breast cancer recurrence or distant breast cancer recurrence; Contralateral invasive breast cancer; Ipsilateral or contralateral Ductal carcinoma in situ or Death only from breast cancer cause.
Time Frame	Event driven (until data cutoff: 29 February 2012: up to 49 months)
Safety Issue?	No

Analysis Population Description
Intent-to-treat participants, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy alone

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290
Time to Breast Cancer-Free Interval (BCFI) Event [units: Months] Median (95% Confidence Interval)	NA (NA to NA) [1]	NA (NA to NA) [1]

[1] The median was not reached.

Statistical Analysis 1 for Time to Breast Cancer-Free Interval (BCFI) Event

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

Statistical Test of Hypothesis	P-Value	0.2792
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.89
	Confidence Interval	(2-Sided) 95% 0.72 to 1.10
	Estimation Comments	Stratification factors were axillary nodal status, choice of adjuvant chemotherapy, hormone receptor status, surgery.

10. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Breast Cancer-Free Interval (BCFI) Events
Measure Description	BCFI is defined as the time from randomization until the date of the first occurrence of one of the following events: Ipsilateral local/regional invasive breast cancer recurrence or distant breast cancer recurrence; Contralateral invasive breast cancer; Ipsilateral or contralateral DCIS or Death only from breast cancer cause. Percentage of participants with and without BCFI events by the time of the data cutoff is presented.

Time Frame	Event driven (until data cutoff: 29 February 2012: up to 49 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy alone

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290
Percentage of Participants With Breast Cancer-Free Interval (BCFI) Events [units: Percentage of participants]		
Percentage of Participants with Events	13.2	14.2
Percentage of Participants without Events	86.8	85.8

11. Secondary Outcome Measure:

Measure Title	Time to Disease-Free Survival (DFS) Event
Measure Description	DFS is defined as the time from randomization until the date of the first occurrence of one of the following events: Ipsilateral invasive breast cancer recurrence (same breast); Ipsilateral (same side of body) local regional invasive breast cancer recurrence (axilla, regional lymph nodes, chest wall, and/or skin); Distant recurrence (evidence of breast cancer in any anatomic site); Death attributable to any cause; Contralateral (opposite side of the body) invasive breast cancer, Second primary non-breast invasive cancer or New diagnosis of an ipsilateral or contralateral Ductal carcinoma in situ (DCIS).
Time Frame	Event driven (until data cutoff: 29 February 2012: up to 49 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy alone

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290
Time to Disease-Free Survival (DFS) Event [units: Months] Median (95% Confidence Interval)	NA (NA to NA) [1]	NA (NA to NA) [1]

[1] The median was not reached.

Statistical Analysis 1 for Time to Disease-Free Survival (DFS) Event

Statistical Analysis Overview	Comparison Groups	Bevacizumab and Chemotherapy, Chemotherapy
	Comments	[Not specified]
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]
Statistical Test of Hypothesis	P-Value	0.1832
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]
Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.87
	Confidence Interval	(2-Sided) 95% 0.72 to 1.07
	Estimation Comments	Stratification factors were axillary nodal status, choice of adjuvant chemotherapy, hormone receptor status, surgery.

12. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Disease-Free Survival (DFS) Events
Measure Description	DFS is defined as the time from randomization until the date of the first occurrence of one of the following events: Ipsilateral invasive breast cancer recurrence (same breast); Ipsilateral (same side of body) local regional invasive breast cancer recurrence (axilla, regional lymph nodes, chest wall, and/or skin); Distant recurrence (evidence of breast cancer in any anatomic site); Death attributable to any cause; Contralateral (opposite side of the body) invasive breast cancer, Second primary non-breast invasive cancer or New diagnosis of an ipsilateral or contralateral Ductal carcinoma in situ (DCIS). Percentage of Participants with and without DFI Events by the time of the data cut-off is presented.
Time Frame	Event driven (until data cutoff: 29 February 2012: up to 49 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy alone

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290
Percentage of Participants With Disease-Free Survival (DFS) Events [units: Percentage of participants]		
with Events	14.7	16.1
without Events	85.3	83.9

13. Secondary Outcome Measure:

Measure Title	Time to Distant Disease-Free Survival (DDFS) Event
Measure Description	DDFS is defined as the time from randomization until the date of the first occurrence of one of the following events: Distant recurrence; Death attributable to any cause; Second primary non-breast invasive cancer (with the exception of non-melanoma Skin cancers).
Time Frame	Event driven (until data cutoff: 29 February 2012: up to 49 months)

Safety Issue?	No

Analysis Population Description

Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy alone

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290
Time to Distant Disease-Free Survival (DDFS) Event [units: Months] Median (95% Confidence Interval)	NA (NA to NA) [1]	NA (NA to NA) [2]

[1] The median was not reached.

[2] The median was not reached

Statistical Analysis 1 for Time to Distant Disease-Free Survival (DDFS) Event

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

Statistical Test of Hypothesis	P-Value	0.3309
	Comments	[Not specified]
	Method	Log Rank
	Comments	[Not specified]

Method of Estimation	Estimation Parameter	Hazard Ratio (HR)
	Estimated Value	0.90
	Confidence Interval	(2-Sided) 95%

		0.72 to 1.12
	Estimation Comments	Stratification factors were axillary nodal status, choice of adjuvant chemotherapy, hormone receptor status, surgery.

14. Secondary Outcome Measure:

Measure Title	Percentage of Participants With Distant Disease-Free Survival (DDFS) Events
Measure Description	DDFS is defined as the time from randomization until the date of the first occurrence of one of the following events: Distant recurrence; Death attributable to any cause; Second primary non-breast invasive cancer (with the exception of non-melanoma Skin cancers). Percentage of participants with and without DDFS Events by the time of the data cutoff is presented.
Time Frame	Event driven (until data cutoff: 29 February 2012: up to 49 months)
Safety Issue?	No

Analysis Population Description

Intent-to-treat population, defined as all randomized participants.

Reporting Groups

	Description
Bevacizumab and Chemotherapy	Participants randomized to receive bevacizumab and chemotherapy
Chemotherapy	Participants randomized to receive chemotherapy alone

Measured Values

	Bevacizumab and Chemotherapy	Chemotherapy
Number of Participants Analyzed	1301	1290
Percentage of Participants With Distant Disease-Free Survival (DDFS) Events [units: Percentage of participants]		
Percentage of Participants with Events	11.7	12.7
Percentage of Participants without Events	88.3	87.3

15. Secondary Outcome Measure:

Measure Title	Number of Participants With Serious Adverse Events (SAEs), Adverse Events (AEs) and Deaths

Measure Description	An adverse event was considered any unfavorable and unintended sign, symptom, or disease associated with the use of the study drug, whether or not considered related to the study drug. Preexisting conditions that worsened during the study were reported as adverse events. A serious adverse event is any experience that suggests a significant hazard, contraindication, side effect or precaution that: results in death, is Life-Threatening, required in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect or is medically significant.
Time Frame	Through end of study: 30 June 2014: up to 77 months
Safety Issue?	No

Analysis Population Description

Safety population, defined as all randomized participants who received at least one dose of study drug. Participants who received at least one full or partial dose of bevacizumab were included in the bevacizumab and chemotherapy arm; all other patients were analyzed in the chemotherapy arm.

Reporting Groups

	Description
Bevacizumab and Chemotherapy (0-18 Months)	Occurring in participants who received bevacizumab and chemotherapy, 0-18 months after first dose
Chemotherapy (0-18 Months)	Occurring in participants who received chemotherapy alone, 0-18 months after first dose
Bevacizumab and Chemotherapy (>18 Months)	Occurring in participants who received bevacizumab and chemotherapy, more than 18 months after first dose
Chemotherapy (>18 Months)	Occurring in participants who received chemotherapy alone, more than 18 months after first dose

Measured Values

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
Number of Participants Analyzed	1288	1271	1288	1271
Number of Participants With Serious Adverse Events (SAEs), Adverse Events (AEs) and Deaths [units: Participants]				
Serious Adverse Events	379	250	45	48
Adverse Events (5% Reporting Threshold)	1268	1233	0	0
Deaths	31	41	113	106

Reported Adverse Events

Time Frame	Through end of study, 30 June 2014
Additional Description	The analysis set was the safety population, defined as all randomized participants who received at least one dose of study drug. Participants who received at least one full or partial dose of bevacizumab were included in the bevacizumab and chemotherapy arm; all others, in the chemotherapy arm. MedDRA (15.0) and MedDRA (17.0) were used.

Reporting Groups

	Description
Bevacizumab and Chemotherapy (0-18 Months)	Occurring in participants who received bevacizumab and chemotherapy, during treatment period (0-18 months) after first dose
Chemotherapy (0-18 Months)	Occurring in participants who received chemotherapy alone, during treatment period (0-18 months) after first dose
Bevacizumab and Chemotherapy (>18 Months)	Occurring in participants who received bevacizumab and chemotherapy, during follow-up period (>18 months) after first dose
Chemotherapy (>18 Months)	Occurring in participants who received chemotherapy alone, during follow-up period (>18 months) after first dose

Serious Adverse Events

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	379/1288 (29.43%)	250/1271 (19.67%)	45/1288 (3.49%)	48/1271 (3.78%)
Blood and lymphatic system disorders				
Anaemia †	1/1288 (0.08%)	3/1271 (0.24%)	0/1288 (0%)	0/1271 (0%)
Febrile bone marrow aplasia †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Febrile neutropenia †	84/1288 (6.52%)	59/1271 (4.64%)	0/1288 (0%)	0/1271 (0%)
Leukopenia †	8/1288 (0.62%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Neutropenia †	69/1288 (5.36%)	38/1271 (2.99%)	0/1288 (0%)	0/1271 (0%)
Pancytopenia †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Thrombocytopenia †	4/1288 (0.31%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Cardiac disorders				
Acute coronary syndrome †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Acute myocardial infarction †	4/1288 (0.31%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Angina pectoris †	1/1288 (0.08%)	0/1271 (0%)	2/1288 (0.16%)	0/1271 (0%)
Angina unstable [A] †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Arrhythmia †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Arteriosclerosis coronary artery †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Atrial fibrillation †	4/1288 (0.31%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Atrial thrombosis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Cardiac arrest [A] †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Cardiac failure †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Cardiac failure congestive †	6/1288 (0.47%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Cardio-respiratory arrest †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Cardiogenic shock †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Congestive cardiomyopathy †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Coronary artery disease †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Coronary artery stenosis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Left ventricular dysfunction †	4/1288 (0.31%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Left ventricular failure †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Mitral valve disease †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Myocardial infarction †	4/1288 (0.31%)	0/1271 (0%)	2/1288 (0.16%)	1/1271 (0.08%)
Supraventricular tachycardia †	0/1288 (0%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Tachycardia †	0/1288 (0%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Ventricular fibrillation †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	1/1271 (0.08%)
Ear and labyrinth disorders				

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Sudden hearing loss †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Endocrine disorders				
Basedow's disease †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Goitre †	0/1288 (0%)	1/1271 (0.08%)	2/1288 (0.16%)	1/1271 (0.08%)
Hyperparathyroidism primary [A] †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Eye disorders				
Cataract [A] †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Diplopia †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Gaze palsy †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Gastrointestinal disorders				
Abdominal pain †	3/1288 (0.23%)	5/1271 (0.39%)	0/1288 (0%)	0/1271 (0%)
Abdominal pain lower †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Abdominal pain upper †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Anal fissure †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Anal fistula †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Caecitis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Colitis †	1/1288 (0.08%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Constipation †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Crohn's Disease †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Diarrhoea †	4/1288 (0.31%)	3/1271 (0.24%)	0/1288 (0%)	0/1271 (0%)
Diverticular perforation †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Diverticulitis intestinal haemorrhagic †	1/1288 (0.08%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Enterocolonic fistula †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Gastric ulcer haemorrhage †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Gastritis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Gastrointestinal haemorrhage †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Gastrointestinal inflammation †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Gastrooesophageal reflux disease †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Gingival ulceration †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Gingivitis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Haematochezia †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Haemorrhoids †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Ileus †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Inguinal hernia †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Intestinal obstruction †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Nausea †	8/1288 (0.62%)	4/1271 (0.31%)	0/1288 (0%)	0/1271 (0%)
Neutropenic colitis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Oesophagitis †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Pancreatitis †	3/1288 (0.23%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Periodontitis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Proctitis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Rectal haemorrhage †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Rectal polyp †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Stomatitis †	12/1288 (0.93%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Subileus †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Toothache †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Umbilical hernia †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Vomiting †	7/1288 (0.54%)	9/1271 (0.71%)	0/1288 (0%)	0/1271 (0%)
General disorders				
Adverse drug reaction †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Asthenia †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Catheter site haematoma †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Catheter site inflammation †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Catheter site pain †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Chest discomfort †	1/1288 (0.08%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Chest pain †	3/1288 (0.23%)	3/1271 (0.24%)	1/1288 (0.08%)	0/1271 (0%)
Chills †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Device damage †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Device deployment issue †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Device dislocation †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Device extrusion †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Device malfunction †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Extravasation †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Fatigue †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
General physical health deterioration †	5/1288 (0.39%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Lipogranuloma [A] †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Malaise †	2/1288 (0.16%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Multi-organ failure †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Non-cardiac chest pain †	3/1288 (0.23%)	1/1271 (0.08%)	0/1288 (0%)	1/1271 (0.08%)
Oedema peripheral [A] †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Pain †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Patient-device incompatibility †	2/1288 (0.16%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Pyrexia †	21/1288 (1.63%)	19/1271 (1.49%)	0/1288 (0%)	0/1271 (0%)
Thrombosis in device †	2/1288 (0.16%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Hepatobiliary disorders				

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Bile duct stone †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Cholecystitis †	1/1288 (0.08%)	2/1271 (0.16%)	2/1288 (0.16%)	0/1271 (0%)
Cholecystitis acute †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Hepatic lesion †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Hepatitis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Hepatitis acute †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Immune system disorders				
Hypersensitivity †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Infections and infestations				
Abscess limb †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Abscess oral †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Anal abscess †	5/1288 (0.39%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Appendicitis †	1/1288 (0.08%)	0/1271 (0%)	1/1288 (0.08%)	1/1271 (0.08%)
Atypical pneumonia [A] †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Bartholin's abscess †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Breast abscess †	0/1288 (0%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Breast cellulitis †	1/1288 (0.08%)	1/1271 (0.08%)	1/1288 (0.08%)	2/1271 (0.16%)
Breast infection †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Bronchitis †	1/1288 (0.08%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Bronchopneumonia †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Catheter site cellulitis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Catheter site infection †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Cellulitis †	5/1288 (0.39%)	3/1271 (0.24%)	0/1288 (0%)	2/1271 (0.16%)
Chronic sinusitis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Clostridium difficile colitis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Cystitis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Device related infection †	9/1288 (0.7%)	4/1271 (0.31%)	0/1288 (0%)	0/1271 (0%)
Diverticulitis †	4/1288 (0.31%)	5/1271 (0.39%)	0/1288 (0%)	1/1271 (0.08%)
Enterocolitis infectious †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Erysipelas †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Escherichia sepsis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Febrile infection †	2/1288 (0.16%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Gastroenteritis †	1/1288 (0.08%)	2/1271 (0.16%)	0/1288 (0%)	1/1271 (0.08%)
Gastroenteritis norovirus †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Gastrointestinal infection †	2/1288 (0.16%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Groin abscess †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
H1N1 influenza †	3/1288 (0.23%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Herpes zoster †	1/1288 (0.08%)	3/1271 (0.24%)	0/1288 (0%)	0/1271 (0%)
Herpes zoster disseminated †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Infection †	14/1288 (1.09%)	3/1271 (0.24%)	0/1288 (0%)	1/1271 (0.08%)
Lower respiratory tract infection †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Lymph node abscess †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Mastitis †	2/1288 (0.16%)	2/1271 (0.16%)	2/1288 (0.16%)	1/1271 (0.08%)
Meningitis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Nasopharyngitis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Neutropenic infection †	8/1288 (0.62%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Neutropenic sepsis †	13/1288 (1.01%)	11/1271 (0.87%)	0/1288 (0%)	0/1271 (0%)
Oesophageal candidiasis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Osteomyelitis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Otitis externa †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Peritonsillitis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Pharyngitis †	3/1288 (0.23%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Pilonidal cyst †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Pneumocystis jiroveci pneumonia †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Pneumonia †	7/1288 (0.54%)	6/1271 (0.47%)	0/1288 (0%)	0/1271 (0%)
Pneumonia bacterial †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Post procedural infection †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Postoperative wound infection †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Pseudomonal sepsis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Rectal abscess †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Respiratory tract infection †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Salpingo-oophoritis [A] †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Sepsis †	4/1288 (0.31%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Sinusitis †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Skin infection †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Staphylococcal infection †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Tonsillitis [A] †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Tooth infection †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Tuberculosis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Upper respiratory tract infection †	0/1288 (0%)	3/1271 (0.24%)	0/1288 (0%)	0/1271 (0%)
Urinary tract infection †	4/1288 (0.31%)	2/1271 (0.16%)	0/1288 (0%)	1/1271 (0.08%)
Wound abscess †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Wound infection †	3/1288 (0.23%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Injury, poisoning and procedural complications				
Ankle fracture †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	1/1271 (0.08%)

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Cervical vertebral fracture †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Contusion [A] †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Coronary artery restenosis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Fall [A] †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Femoral neck fracture †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	1/1271 (0.08%)
Forearm fracture †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Fracture [A] †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Head injury †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Hip fracture †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Humerus fracture †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
In-stent coronary artery restenosis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Injury [A] †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Ligament rupture †	0/1288 (0%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Multiple injuries [A] †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Periprosthetic fracture †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Procedural complication [A] †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Pubis fracture †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Radiation pneumonitis †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Radiation skin injury †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Radius fracture †	1/1288 (0.08%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Rib fracture †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Road traffic accident †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Tibia fracture †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Wound †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Wound complication †	2/1288 (0.16%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Wound dehiscence †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Investigations				
Blood pressure decreased †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Cytology abnormal †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Ejection fraction decreased †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Electrocardiogram QT prolonged †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Gamma-glutamyltransferase increased †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Haemoglobin decreased †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Influenza A virus test positive †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Liver function test abnormal †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Metabolism and nutrition disorders				
Decreased appetite †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Dehydration †	5/1288 (0.39%)	7/1271 (0.55%)	0/1288 (0%)	0/1271 (0%)
Hyperglycaemia †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Hypokalaemia †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Hyponatraemia †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Musculoskeletal and connective tissue disorders				
Arthralgia †	2/1288 (0.16%)	0/1271 (0%)	3/1288 (0.23%)	0/1271 (0%)
Arthritis †	2/1288 (0.16%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Back pain †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Bone pain †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Intervertebral disc disorder [A] †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Intervertebral disc protrusion †	2/1288 (0.16%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Musculoskeletal pain †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Myalgia †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Neck pain †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Osteonecrosis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	1/1271 (0.08%)
Pain in extremity †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Antiomyolipoma †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Basal cell carcinoma †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Benign breast neoplasm †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Bowen's disease †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Haemangioma †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Leiomyoma †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Meningioma †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Oesophageal neoplasm †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Ovarian fibroma †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Squamous cell carcinoma of skin †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Uterine Leiomyoma †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Nervous system disorders				
Carpal tunnel syndrome †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Cerebral ischaemia †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Cerebrovascular accident †	0/1288 (0%)	1/1271 (0.08%)	1/1288 (0.08%)	0/1271 (0%)
Convulsion †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Dizziness †	1/1288 (0.08%)	1/1271 (0.08%)	1/1288 (0.08%)	0/1271 (0%)
Headache †	3/1288 (0.23%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Hypoaesthesia [A] †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Hypoxic-ischaemic encephalopathy †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Loss of consciousness †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	1/1271 (0.08%)
Neuropathy peripheral †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Posterior reversible encephalopathy syndrome †	2/1288 (0.16%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Presyncope [A] †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Sciatica †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Syncope †	5/1288 (0.39%)	2/1271 (0.16%)	0/1288 (0%)	1/1271 (0.08%)
Transient ischaemic attack †	3/1288 (0.23%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Pregnancy, puerperium and perinatal conditions				
Abortion spontaneous [A] †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Hyperemesis gravidarum †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Premature delivery †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Psychiatric disorders				
Agitation †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Anxiety †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Conversion disorder [A] †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	1/1271 (0.08%)
Depression †	1/1288 (0.08%)	1/1271 (0.08%)	1/1288 (0.08%)	1/1271 (0.08%)
Disorientation †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Panic attack †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Psychotic disorder †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Suicide attempt †	2/1288 (0.16%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Renal and urinary disorders				
Calculus ureteric †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
IGA nephropathy †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Renal failure acute †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Stress urinary incontinence †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Reproductive system and breast disorders				
Adenomyosis †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Bartholin's cyst †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Breast calcifications †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Breast cyst †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Breast haematoma †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Breast mass †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Dysfunctional uterine bleeding †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Endometrial hyperplasia †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Endometriosis †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	1/1271 (0.08%)
Menorrhagia †	1/1288 (0.08%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Metrorrhagia †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Ovarian cyst †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Uterine prolapse †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Vaginal haemorrhage †	2/1288 (0.16%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Vaginal prolapse †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Vaginal ulceration †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Asthma †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Atelectasis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Bronchospasm †	2/1288 (0.16%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Dyspnoea †	6/1288 (0.47%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Dyspnoea exertional †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Epistaxis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Haemoptysis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Hyperventilation †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	1/1271 (0.08%)
Interstitial lung disease †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Lung disorder †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Nasal septum perforation †	2/1288 (0.16%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Pharyngeal inflammation †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Pleural effusion †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Pneumonitis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Pneumothorax †	5/1288 (0.39%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Pulmonary artery thrombosis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Pulmonary embolism †	3/1288 (0.23%)	7/1271 (0.55%)	0/1288 (0%)	0/1271 (0%)
Vocal cord polyp †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Skin and subcutaneous tissue disorders				
Dermatitis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Hypertrophic scar [A] †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Palmar-plantar erythrodysaesthesia syndrome †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Pruritus generalised †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Rash †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Rash pruritic †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Skin lesion †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Skin necrosis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Surgical and medical procedures				
Breast prosthesis implantation †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Hysterectomy †	0/1288 (0%)	0/1271 (0%)	0/1288 (0%)	1/1271 (0.08%)
Rehabilitation therapy †	0/1288 (0%)	0/1271 (0%)	1/1288 (0.08%)	0/1271 (0%)
Vascular disorders				
Arterial thrombosis †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Deep vein thrombosis †	6/1288 (0.47%)	5/1271 (0.39%)	0/1288 (0%)	1/1271 (0.08%)
Haematoma [A] †	0/1288 (0%)	0/1271 (0%)	2/1288 (0.16%)	0/1271 (0%)
Hypertension †	7/1288 (0.54%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Hypertensive crisis †	1/1288 (0.08%)	0/1271 (0%)	0/1288 (0%)	0/1271 (0%)
Hypotension †	0/1288 (0%)	2/1271 (0.16%)	0/1288 (0%)	0/1271 (0%)
Shock †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Thrombophlebitis superficial †	1/1288 (0.08%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)
Venous thrombosis †	0/1288 (0%)	3/1271 (0.24%)	0/1288 (0%)	0/1271 (0%)
Venous thrombosis limb †	0/1288 (0%)	1/1271 (0.08%)	0/1288 (0%)	0/1271 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (16.0)

Other Adverse Events

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

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	1268/1288 (98.45%)	1233/1271 (97.01%)	0/1288 (0%)	0/1271 (0%)
Blood and lymphatic system disorders				
Anaemia †	140/1288 (10.87%)	175/1271 (13.77%)	/	/
Leukopenia †	210/1288 (16.3%)	215/1271 (16.92%)	/	/
Neutropenia †	503/1288 (39.05%)	479/1271 (37.69%)	/	/

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Cardiac disorders				
Left ventricular dysfunction †	261/1288 (20.26%)	165/1271 (12.98%)	/	/
Eye disorders				
Lacrimation increased †	156/1288 (12.11%)	109/1271 (8.58%)	/	/
Gastrointestinal disorders				
Abdominal pain †	123/1288 (9.55%)	124/1271 (9.76%)	/	/
Abdominal pain upper †	138/1288 (10.71%)	112/1271 (8.81%)	/	/
Constipation †	444/1288 (34.47%)	401/1271 (31.55%)	/	/
Diarrhoea †	418/1288 (32.45%)	350/1271 (27.54%)	/	/
Dry mouth †	61/1288 (4.74%)	76/1271 (5.98%)	/	/
Dyspepsia †	201/1288 (15.61%)	165/1271 (12.98%)	/	/
Gingival bleeding †	138/1288 (10.71%)	10/1271 (0.79%)	/	/
Haemorrhoids †	78/1288 (6.06%)	58/1271 (4.56%)	/	/
Nausea †	881/1288 (68.4%)	880/1271 (69.24%)	/	/
Stomatitis †	663/1288 (51.48%)	469/1271 (36.9%)	/	/
Vomiting †	480/1288 (37.27%)	459/1271 (36.11%)	/	/
General disorders				
Asthenia †	230/1288 (17.86%)	223/1271 (17.55%)	/	/
Fatigue †	533/1288 (41.38%)	539/1271 (42.41%)	/	/
Influenza like illness †	68/1288 (5.28%)	61/1271 (4.8%)	/	/
Oedema peripheral †	145/1288 (11.26%)	164/1271 (12.9%)	/	/
Pain †	72/1288 (5.59%)	58/1271 (4.56%)	/	/
Pyrexia †	214/1288 (16.61%)	164/1271 (12.9%)	/	/
Infections and infestations				
Nasopharyngitis †	137/1288 (10.64%)	125/1271 (9.83%)	/	/

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Upper respiratory tract infection †	103/1288 (8%)	109/1271 (8.58%)	/	/
Urinary tract infection †	95/1288 (7.38%)	100/1271 (7.87%)	/	/
Injury, poisoning and procedural complications				
Radiation skin injury †	151/1288 (11.72%)	190/1271 (14.95%)	/	/
Investigations				
Alanine aminotransferase increased †	67/1288 (5.2%)	50/1271 (3.93%)	/	/
Aspartate aminotransferase increased †	84/1288 (6.52%)	49/1271 (3.86%)	/	/
Ejection fraction decreased †	103/1288 (8%)	71/1271 (5.59%)	/	/
Gamma-glutamyltransferase increased †	82/1288 (6.37%)	45/1271 (3.54%)	/	/
Weight decreased †	72/1288 (5.59%)	28/1271 (2.2%)	/	/
Metabolism and nutrition disorders				
Decreased appetite †	260/1288 (20.19%)	223/1271 (17.55%)	/	/
Musculoskeletal and connective tissue disorders				
Arthralgia †	414/1288 (32.14%)	252/1271 (19.83%)	/	/
Back pain †	172/1288 (13.35%)	141/1271 (11.09%)	/	/
Bone pain †	99/1288 (7.69%)	111/1271 (8.73%)	/	/
Musculoskeletal pain †	162/1288 (12.58%)	123/1271 (9.68%)	/	/
Myalgia †	278/1288 (21.58%)	273/1271 (21.48%)	/	/
Pain in extremity †	198/1288 (15.37%)	171/1271 (13.45%)	/	/
Nervous system disorders				
Dizziness †	130/1288 (10.09%)	121/1271 (9.52%)	/	/
Dysgeusia †	243/1288 (18.87%)	230/1271 (18.1%)	/	/
Headache †	440/1288 (34.16%)	289/1271 (22.74%)	/	/
Neuropathy peripheral †	138/1288 (10.71%)	135/1271 (10.62%)	/	/
Paraesthesia †	88/1288 (6.83%)	91/1271 (7.16%)	/	/

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Peripheral sensory neuropathy †	137/1288 (10.64%)	128/1271 (10.07%)	/	/
Psychiatric disorders				
Anxiety †	88/1288 (6.83%)	78/1271 (6.14%)	/	/
Depression †	57/1288 (4.43%)	69/1271 (5.43%)	/	/
Insomnia †	191/1288 (14.83%)	217/1271 (17.07%)	/	/
Renal and urinary disorders				
Proteinuria †	195/1288 (15.14%)	24/1271 (1.89%)	/	/
Reproductive system and breast disorders				
Breast pain †	60/1288 (4.66%)	86/1271 (6.77%)	/	/
Respiratory, thoracic and mediastinal disorders				
Cough †	215/1288 (16.69%)	161/1271 (12.67%)	/	/
Dysphonia †	99/1288 (7.69%)	19/1271 (1.49%)	/	/
Dyspnoea †	144/1288 (11.18%)	123/1271 (9.68%)	/	/
Epistaxis †	478/1288 (37.11%)	75/1271 (5.9%)	/	/
Oropharyngeal pain †	179/1288 (13.9%)	99/1271 (7.79%)	/	/
Rhinorrhoea †	104/1288 (8.07%)	65/1271 (5.11%)	/	/
Skin and subcutaneous tissue disorders				
Alopecia †	807/1288 (62.66%)	833/1271 (65.54%)	/	/
Dry skin †	70/1288 (5.43%)	72/1271 (5.66%)	/	/
Erythema †	86/1288 (6.68%)	114/1271 (8.97%)	/	/
Nail disorder †	183/1288 (14.21%)	150/1271 (11.8%)	/	/
Palmar-Plantar erythrodysaesthesia syndrome †	92/1288 (7.14%)	70/1271 (5.51%)	/	/
Pruritus †	71/1288 (5.51%)	63/1271 (4.96%)	/	/
Rash †	160/1288 (12.42%)	137/1271 (10.78%)	/	/

	Bevacizumab and Chemotherapy (0-18 Months)	Chemotherapy (0-18 Months)	Bevacizumab and Chemotherapy (>18 Months)	Chemotherapy (>18 Months)
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Skin hyperpigmentation †	68/1288 (5.28%)	49/1271 (3.86%)	/	/
Vascular disorders				
Hot flush †	206/1288 (15.99%)	208/1271 (16.37%)	/	/
Hypertension †	456/1288 (35.4%)	65/1271 (5.11%)	/	/
Lymphoedema †	70/1288 (5.43%)	74/1271 (5.82%)	/	/

† Indicates events were collected by systematic assessment.

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.

Results Point of Contact:

Name/Official Title: Medical Communications
Organization: Hoffman-LaRoche
Phone: 800-821-8590
Email: