ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 06/30/2014

# A Study of Avastin (Bevacizumab) in Combination With Chemotherapy in Patients With Primary Breast Cancer

This study has been completed.

| | |
|---|---|
| Sponsor: | Hoffmann-La Roche |
| Collaborators: | |
| Information provided by (Responsible Party): | Hoffmann-La Roche |
| ClinicalTrials.gov Identifier: | NCT02005549 |

## Purpose

This study will evaluate the effect of Avastin (15mg/kg iv) in combination with Docetaxel and Xeloda, given as pre-operative therapy to patients with primary breast cancer. Avastin will be administered every 3 weeks, for the first 5 cycles of chemotherapy. The anticipated time on study treatment is 3-12 months.

| Condition | Intervention | Phase |
|---|---|---|
| Breast Cancer | Drug: bevacizumab [Avastin]<br>Drug: docetaxel<br>Drug: capecitabine [Xeloda] | Phase 2 |

Study Type: Interventional
Study Design: Treatment, Single Group Assignment, Open Label, Non-Randomized, Safety/Efficacy Study
Official Title: A Phase II Study of Bevacizumab With Docetaxel and Capecitabine in the Neoadjuvant Setting for Breast Cancer Patients

Further study details as provided by Hoffmann-La Roche:

Primary Outcome Measure:

- Percentage of Participants With Pathological Complete Response (pCR) [Time Frame: Baseline, 20-24 weeks (final surgery, performed 2 to 4 weeks after the last chemotherapy cycle [Week 18])] [Designated as safety issue: No]
  pCR was defined as the absence of signs for invasive tumor in the final surgical sample as judged by the local pathologist. Surgery was performed 2 to 4 weeks after the last chemotherapy cycle.

Secondary Outcome Measures:

- Percentage of Participants With pCR, Clinical Complete Response (CR), or Clinical Partial Response (PR) [Time Frame: Baseline, 20-24 weeks (final surgery, performed 2 to 4 weeks after the last chemotherapy cycle [Week 18])] [Designated as safety issue: No]
  Percentage of participants with pCR plus the percentage of participants without pCR who achieved CR or PR as measured by the Response Evaluation Criteria in Solid Tumors (RECIST) criteria. CR was defined as complete disappearance of all target lesions and non-target disease, with the exception of nodal disease. All nodes, both target and non-target, must have decreased to normal (short axis less than [<] 10 millimeters [mm]). No new lesions. PR was defined as greater than or equal to (≥) 30 percent (%) decrease under baseline of the sum of diameters of all target lesions. The short axis was used in the sum for target nodes, while the longest diameter was used in the sum for all other target lesions. No unequivocal progression of non-target disease. No new lesions.
- Percentage of Participants Undergoing Breast-Conserving Surgery [Time Frame: 20-24 weeks (final surgery, performed 2 to 4 weeks after the last chemotherapy cycle [Week 18])] [Designated as safety issue: No]
  Percentage of participants undergoing a breast-conserving procedure versus a modified radical mastectomy at final surgery, performed 2 to 4 weeks after the last chemotherapy cycle (Week 18)

Enrollment: 18
Study Start Date: February 2006
Primary Completion Date: April 2008
Study Completion Date: April 2008

| Arms | Assigned Interventions |
|---|---|
| Experimental: Neoadjuvant Therapy | Drug: bevacizumab [Avastin]<br>15 mg/kg iv on Day 1 of each 3-week cycle, 5 cycles<br><br>Drug: docetaxel<br>75 mg/m2 on Day 1 of each 3-week cycle, 6 cycles<br><br>Drug: capecitabine [Xeloda]<br>950 mg/m2, orally twice daily, evening of Day 1 until morning of Day 15, followed by a 7 day rest period, every 3 weeks |

## Eligibility

Ages Eligible for Study: 18 Years to 70 Years
Genders Eligible for Study: Female
Accepts Healthy Volunteers: No

### Criteria

Inclusion Criteria:

- female patients, 18-70years of age;
- histologically-proven invasive breast cancer;
- no prior or current neoplasm except for non-melanoma skin cancer, or in situ cancer of the cervix;
- no distant disease/secondary cancer.

Exclusion Criteria:

- pregnant or lactating women;
- pre-operative local treatment for breast cancer;
- prior or concurrent systemic antitumor therapy;
- clinically significant cardiac disease.

## Contacts and Locations

Locations

Austria

Salzburg, Austria, 5020

Investigators

| | | |
|---|---|---|
| Study Chair: | Clinical Trials | Hoffmann-La Roche |

## More Information

| | |
|---|---|
| Responsible Party: | Hoffmann-La Roche |
| Study ID Numbers: | ML19869 |
| Health Authority: | Austria: Austrian Federal Office for Safety in Health Care |

# Study Results

## Participant Flow

Reporting Groups

| | Description |
|---|---|
| Bevacizumab+Docetaxel +Capecitabine | Participants received bevacizumab, 15 milligrams/kilogram (mg/kg) intravenously (IV), followed by docetaxel 75 mg per square meter (mg/m^2) IV on Day 1 and capecitabine 950 mg/m^2 orally (PO) twice daily (BID) within 30 minutes after the end of a meal, starting the evening of Day 1 and continuing until the morning of Day 15 (followed by a 7-day rest period) for a maximum of five 3-week cycles. |

Overall Study

| | Bevacizumab+Docetaxel+Capecitabine |
|---|---|
| Started | 18 |
| Completed | 18 |
| Not Completed | 0 |

## Baseline Characteristics

Analysis Population Description

Intent-to-treat (ITT) population. All participants who received at least one dose of study drug.

Reporting Groups

| | Description |
|---|---|
| Bevacizumab+Docetaxel +Capecitabine | Participants received bevacizumab, 15 mg/kg IV, followed by docetaxel 75 mg/m^2 IV on Day 1 and capecitabine 950 mg/m^2 PO BID within 30 minutes after the end of a meal, starting the evening of Day 1 and continuing until the morning of Day 15 (followed by a 7-day rest period) for a maximum of five 3-week cycles. |

Baseline Measures

| | Bevacizumab+Docetaxel+Capecitabine |
|---|---|
| Number of Participants | 18 |
| Age, Continuous [units: years] Median (Full Range) | 48 (34 to 69) |
| Gender, Male/Female [units: participants] | |
| Female | 18 |
| Male | 0 |

## Outcome Measures

1. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | Percentage of Participants With Pathological Complete Response (pCR) |
| Measure Description | pCR was defined as the absence of signs for invasive tumor in the final surgical sample as judged by the local pathologist. Surgery was performed 2 to 4 weeks after the last chemotherapy cycle. |
| Time Frame | Baseline, 20-24 weeks (final surgery, performed 2 to 4 weeks after the last chemotherapy cycle [Week 18]) |
| Safety Issue? | No |

Analysis Population Description

ITT population; participants evaluable for response included those participants who received a minimum of 3 cycles of treatment (9 weeks on study) with final surgery performed and the samples and reports available.

Reporting Groups

| | Description |
|---|---|
| Bevacizumab+Docetaxel +Capecitabine | Participants received bevacizumab, 15 mg/kg IV, followed by docetaxel 75 mg/m^2 IV on Day 1 and capecitabine 950 mg/m^2 PO BID within 30 minutes after the end of a meal, starting the evening of Day 1 and continuing until the morning of Day 15 (followed by a 7-day rest period) for a maximum of five 3-week cycles. |

Measured Values

| | Bevacizumab+Docetaxel+Capecitabine |
|---|---|
| Number of Participants Analyzed | 18 |
| Percentage of Participants With Pathological Complete Response (pCR)<br>[units: percentage of participants]<br>Number (95% Confidence Interval) | 22.22 (6.41 to 47.64) |

2. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Percentage of Participants With pCR, Clinical Complete Response (CR), or Clinical Partial Response (PR) |
| Measure Description | Percentage of participants with pCR plus the percentage of participants without pCR who achieved CR or PR as measured by the Response Evaluation Criteria in Solid Tumors (RECIST) criteria. CR was defined as complete disappearance of all target lesions and non-target disease, with the exception of nodal disease. All nodes, both target and non-target, must have decreased to normal (short axis less than [<] 10 millimeters [mm]). No new lesions. PR was defined as greater than or equal to (≥) 30 percent (%) decrease under baseline of the sum of diameters of all target lesions. The short axis was used in the sum for target nodes, while the longest diameter was used in the sum for all other target lesions. No unequivocal progression of non-target disease. No new lesions. |
| Time Frame | Baseline, 20-24 weeks (final surgery, performed 2 to 4 weeks after the last chemotherapy cycle [Week 18]) |
| Safety Issue? | No |

Analysis Population Description

ITT population; participants evaluable for response included those participants who received a minimum of 3 cycles of treatment (9 weeks on study) with final surgery performed and the samples and reports available.

Reporting Groups

| | Description |
|---|---|
| Bevacizumab+Docetaxel +Capecitabine | Participants received bevacizumab, 15 mg/kg IV, followed by docetaxel 75 mg/m^2 IV on Day 1 and capecitabine 950 mg/m^2 PO BID within 30 minutes after the end of a meal, starting the evening of Day 1 and continuing until the morning of Day 15 (followed by a 7-day rest period) for a maximum of five 3-week cycles. |

Measured Values

| | Bevacizumab+Docetaxel+Capecitabine |
|---|---|
| Number of Participants Analyzed | 18 |
| Percentage of Participants With pCR, Clinical Complete Response (CR), or Clinical Partial Response (PR)<br>[units: percentage of participants]<br>Number (95% Confidence Interval) | 72.22 (46.52 to 90.31) |

3. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Percentage of Participants Undergoing Breast-Conserving Surgery |
| Measure Description | Percentage of participants undergoing a breast-conserving procedure versus a modified radical mastectomy at final surgery, performed 2 to 4 weeks after the last chemotherapy cycle (Week 18) |
| Time Frame | 20-24 weeks (final surgery, performed 2 to 4 weeks after the last chemotherapy cycle [Week 18]) |
| Safety Issue? | No |

Analysis Population Description

ITT population.

Reporting Groups

| | Description |
|---|---|
| Bevacizumab+Docetaxel +Capecitabine | Participants received bevacizumab, 15 mg/kg IV, followed by docetaxel 75 mg/m^2 IV on Day 1 and capecitabine 950 mg/m^2 PO BID within 30 minutes after the end of a meal, starting the evening of Day 1 and continuing until the morning of Day 15 (followed by a 7-day rest period) for a maximum of five 3-week cycles. |

Measured Values

| | Bevacizumab+Docetaxel+Capecitabine |
|---|---|
| Number of Participants Analyzed | 18 |
| Percentage of Participants Undergoing Breast-Conserving Surgery<br>[units: percentage of participants]<br>Number (95% Confidence Interval) | 83 (59 to 96) |

## Reported Adverse Events

| | |
|---|---|
| Time Frame | Baseline, every three weeks (Cycles 1 through 6), end-of-treatment, to 28 days after last dosage of study drug. |
| Additional Description | An adverse event is any undesirable event associated with the use of a drug, whether or not considered drug related, and includes any side effect, injury, toxicity, or sensitivity reactions. It also includes any undesirable clinical or laboratory event which is not normally observed in the participant. |

Reporting Groups

| | Description |
|---|---|
| Bevacizumab+Docetaxel +Capecitabine | Participants received bevacizumab, 15 mg/kg IV, followed by docetaxel 75 mg/m^2 IV on Day 1 and capecitabine 950 mg/m^2 PO BID within 30 minutes after the end of a meal, starting the evening of Day 1 and continuing until the morning of Day 15 (followed by a 7-day rest period) for a maximum of five 3-week cycles. |

Serious Adverse Events

| | Bevacizumab+Docetaxel+Capecitabine |
|---|---|
| | Affected/At Risk (%) |
| Total | 5/18 (27.78%) |
| Gastrointestinal disorders | |
| Intestinal perforation [A] * | 1/18 (5.56%) |
| General disorders | |
| General physical health deterioration [A] * | 1/18 (5.56%) |
| Impaired healing [A] * | 1/18 (5.56%) |
| Infections and infestations | |
| Neutropenic infection [A] * | 1/18 (5.56%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | |
| Contralateral breast cancer [A] * | 1/18 (5.56%) |
| Reproductive system and breast disorders | |
| Menorrhagia [A] * | 1/18 (5.56%) |
| Vascular disorders | |
| Deep vein thrombosis [A] * | 2/18 (11.11%) |

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA

Other Adverse Events

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

| | Bevacizumab+Docetaxel+Capecitabine |
|---|---|
| | Affected/At Risk (%) |
| Total | 18/18 (100%) |
| Blood and lymphatic system disorders | |
| Anaemia [A] * | 5/18 (27.78%) |
| Leukopenia [A] * | 3/18 (16.67%) |
| Lymphopenia [A] * | 8/18 (44.44%) |
| Neutropenia [A] * | 3/18 (16.67%) |
| Cardiac disorders | |
| Cardiovascular disorder [A] * | 1/18 (5.56%) |
| Pericardial effusion [A] * | 1/18 (5.56%) |
| Ear and labyrinth disorders | |
| Vertigo [A] * | 2/18 (11.11%) |
| Eye disorders | |
| Conjunctivitis [A] * | 2/18 (11.11%) |
| Visual acuity reduced [A] * | 1/18 (5.56%) |
| Gastrointestinal disorders | |
| Abdominal pain [A] * | 4/18 (22.22%) |
| Abdominal pain upper [A] * | 1/18 (5.56%) |
| Constipation [A] * | 8/18 (44.44%) |
| Diarrhoea [A] * | 4/18 (22.22%) |
| Dry mouth [A] * | 1/18 (5.56%) |

| | Bevacizumab+Docetaxel+Capecitabine |
|---|---|
| | Affected/At Risk (%) |
| Duodenitis [A] * | 1/18 (5.56%) |
| Dyspepsia [A] * | 1/18 (5.56%) |
| Eructation [A] * | 1/18 (5.56%) |
| Gastritis [A] * | 1/18 (5.56%) |
| Intestinal perforation [A] * | 1/18 (5.56%) |
| Melaena [A] * | 1/18 (5.56%) |
| Nausea [A] * | 3/18 (16.67%) |
| Oral pain [A] * | 1/18 (5.56%) |
| Stomatitis [A] * | 5/18 (27.78%) |
| Vomiting [A] * | 1/18 (5.56%) |
| General disorders | |
| Asthenia [A] * | 1/18 (5.56%) |
| Fatigue [A] * | 6/18 (33.33%) |
| General physical health deterioration [A] * | 1/18 (5.56%) |
| Impaired healing [A] * | 1/18 (5.56%) |
| Mucosal inflammation [A] * | 1/18 (5.56%) |
| Oedema peripheral [A] * | 1/18 (5.56%) |
| Pyrexia [A] * | 1/18 (5.56%) |
| Infections and infestations | |
| Laryngitis [A] * | 1/18 (5.56%) |
| Nasopharyngitis [A] * | 1/18 (5.56%) |
| Neutropenic infection [A] * | 1/18 (5.56%) |

| | Bevacizumab+Docetaxel+Capecitabine |
|---|---|
| | Affected/At Risk (%) |
| Oral herpes [A] * | 1/18 (5.56%) |
| Rhinitis [A] * | 3/18 (16.67%) |
| Urinary tract infection [A] * | 1/18 (5.56%) |
| Injury, poisoning and procedural complications | |
| Procedural pain [A] * | 1/18 (5.56%) |
| Wound complications [A] * | 1/18 (5.56%) |
| Investigations | |
| Alanine aminotransferased increased [A] * | 1/18 (5.56%) |
| Blood lactate dehydrogenase increased [A] * | 8/18 (44.44%) |
| C-reactive protein increased [A] * | 1/18 (5.56%) |
| Pulse abnormal [A] * | 1/18 (5.56%) |
| Weight decreased [A] * | 5/18 (27.78%) |
| Metabolism and nutrition disorders | |
| Anorexia [A] * | 3/18 (16.67%) |
| Hyperglycaemia [A] * | 8/18 (44.44%) |
| Hypokalaemia [A] * | 2/18 (11.11%) |
| Musculoskeletal and connective tissue disorders | |
| Bone pain [A] * | 1/18 (5.56%) |
| Myalgia [A] * | 1/18 (5.56%) |
| Neck pain [A] * | 1/18 (5.56%) |
| Pain in extremity [A] * | 6/18 (33.33%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | |
| Contralateral breast cancer [A] * | 1/18 (5.56%) |

| | Bevacizumab+Docetaxel+Capecitabine |
|---|---|
| | Affected/At Risk (%) |
| Nervous system disorders | |
| Dysgeusia [A] * | 4/18 (22.22%) |
| Headache [A] * | 3/18 (16.67%) |
| Polyneuropathy [A] * | 4/18 (22.22%) |
| Psychiatric disorders | |
| Anxiety [A] * | 1/18 (5.56%) |
| Depression [A] * | 2/18 (11.11%) |
| Insomnia [A] * | 2/18 (11.11%) |
| Panic attack [A] * | 1/18 (5.56%) |
| Sleep disorder [A] * | 2/18 (11.11%) |
| Reproductive system and breast disorders | |
| Menorrhagia [A] * | 2/18 (11.11%) |
| Pelvic pain [A] * | 1/18 (5.56%) |
| Vaginal haemorrhage [A] * | 1/18 (5.56%) |
| Respiratory, thoracic and mediastinal disorders | |
| Dysphonia [A] * | 2/18 (11.11%) |
| Epistaxis [A] * | 3/18 (16.67%) |
| Skin and subcutaneous tissue disorders | |
| Alopecia [A] * | 17/18 (94.44%) |
| Dry skin [A] * | 1/18 (5.56%) |
| Erythema [A] * | 1/18 (5.56%) |
| Nail disorder [A] * | 12/18 (66.67%) |

| | Bevacizumab+Docetaxel+Capecitabine |
|---|---|
| | Affected/At Risk (%) |
| Palmar-plantar erythrodysaesthesia syndrome [A] * | 3/18 (16.67%) |
| Pruritus [A] * | 1/18 (5.56%) |
| Rash [A] * | 3/18 (16.67%) |
| Vascular disorders | |
| Deep vein thrombosis [A] * | 2/18 (11.11%) |
| Hot flush [A] * | 3/18 (16.67%) |
| Thrombophlebitis [A] * | 1/18 (5.56%) |

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

## Limitations and Caveats

Nonserious adverse events presented in this record include all adverse events reported during the study, not just nonserious events.

## More Information

Certain Agreements:

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

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

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

Results Point of Contact:

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Organization: Hoffmann-LaRoche
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