A Study to Determine the Activity of Caelyx With Trastuzumab and Docetaxel in the Treatment of Metastatic Breast Cancer (Study P03679)

This study has been completed.

Sponsor:
Merck Sharp & Dohme Corp.

Collaborator:
MDS Pharma Services

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT00687440

First received: May 27, 2008
Last updated: October 29, 2014
Last verified: October 2014
History of Changes

Purpose

The purpose of this study is to evaluate, in a first stage, the safety (incidence of cardiac toxicity) of Caelyx in combination with Trastuzumab and Docetaxel; and in a second stage, the tumor response rate of this regimen. This study will be conducted in approximately 30 centers. A total of approximately 70 to 95 subjects will be enrolled.

Condition	Intervention	Phase
Breast Neoplasm	Drug: Pegylated Liposomal Doxorubicin Drug: Docetaxel Drug: Trastuzumab	Phase 2

Study Type: Interventional
Study Design: Endpoint Classification: Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Pegylated Liposomal Doxorubicin (Caelyx) in Combination With Herceptin and Taxotere as First-line Chemotherapy in Metastatic Breast Cancer Patients: A 2 Stage Phase II, Open Label, Multicenter Study.

Resource links provided by NLM:

Genetics Home Reference related topics: breast cancer

MedlinePlus related topics: Breast Cancer Cancer

Drug Information available for: Doxorubicin Doxorubicin hydrochloride Docetaxel Trastuzumab

U.S. FDA Resources

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Number of Participants Who Had a Tumor Response, According to Standard RECIST (Response Evaluation Criteria in Solid Tumors) Criteria [Time Frame: Week 09, Week 18, at the end of each patient's treatment, and at 3, 6, 9, and 12 months after end of treatment.] [Designated as safety issue: No]

  Those who achieved either complete (disappearance of all target lesions) or partial (at least 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum LD) response.

Enrollment:	27
Study Start Date:	May 2005
Study Completion Date:	October 2008
Primary Completion Date:	October 2008 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: Caelyx, Docetaxel, Trastuzumab Stage 1: subjects will receive Caelyx one day every 3 weeks in combination with docetaxel one day every 3 weeks and trastuzumab once weekly during 6 cycles. At the end of this stage, based on the number of cardiac events, subjects will proceed to a second stage or restart with a lower dose of Caelyx. Stage 2: subjects will be treated with the recommended dose of Caelyx (defined in the first stage) in combination with docetaxel and trastuzumab.	Drug: Pegylated Liposomal Doxorubicin Stage 1: 25 subjects will be treated with Caelyx IV 30 mg/m^2 on day 1, every 3 weeks Stage 2: 45 new patients will be treated at the recommended dose level (defined in the first step) on day 1, every 3 weeks. Other Name: Caelyx Drug: Docetaxel Stage 1 and Stage 2: Docetaxel 60 mg/m2 IV as 1-hour infusion, on day 1, every 3 weeks. Other Name: Taxotere Drug: Trastuzumab Stage 1 and Stage 2: 4 mg/kg IV 90-minute infusion loading dose. Then 2 mg/kg IV weekly during 6 cycles (18 weeks).

Eligibility

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

Criteria

Inclusion Criteria:

Patients must fulfill all the following criteria:

- Females aged 18 to 70 years-old.
- Willingness to participate in the study and comply with its procedures.
- Documented diagnosis of metastatic breast carcinoma (stage IV) Human Epidermal Growth Factor Receptor 2 (HER2) overexpressing (Immunohistochemistry (IHC) 3+ or Fluorescence In Situ Hybridization(FISH) +).
- No prior chemotherapy for metastatic breast cancer.
- Adjuvant or neo-adjuvant chemotherapy is allowed according to the following rules:
  - patients treated with anthracyclines if all the following conditions are met:

        - Doxorubicin total dose <= 300 mg/m^2
        - Epirubicin total dose <= 480 mg/m^2
        - Chemotherapy-free interval of > 12 months
    - no taxane-based adjuvant or neo-adjuvant chemotherapy is allowed;
    - patients treated with non-anthracycline/taxane adjuvant or neo-adjuvant chemotherapy regimens are freely eligible (i.e. cyclophosphamide/methotrexate/fluorouracil (CMF) or similar regimens).
- At least one measurable lesion according to RECIST criteria.
- Complete hematologic and biologic baseline evaluation within 2 weeks prior to start of treatment.
- Complete Tumor baseline evaluation including a total body computed tomography (CT) scan within 4 weeks prior to start of treatment.
- Left ventricular ejection fraction (LVEF) >= 50% as determined by echocardiogram or Multi Gated Acquisition (MUGA) scan.
- World Health Organization (WHO) performance status 0,1.
- Life expectancy > 3 months.
- Laboratory requirements :
    - Hematology :
        - Neutrophils > 1.5 x 10^9/L
        - Platelets > 100 x 10^9/L
        - Hemoglobin > 10 g/dL
    - Hepatic function:
        - Total bilirubin <= 1.25 x the upper-normal limits (UNL);
        - ASAT (Aspartate Aminotransferase or SGOT), ALAT (Alanine aminotransferase or SGPT) <= 2.5 x the upper-normal limits;
    - For patients with liver metastases:
        - Total bilirubin < 1.5 x the UNL (Upper limit of normal) ;
        - ASAT and/or ALAT < 3 x the UNL;
    - Renal function :
        - Serum Creatinine < 1.5 x the UNL.
- Women of child bearing potential must have a negative serum pregnancy test and be using adequate contraception.
- Patients must be accessible for treatment and follow-up.

Exclusion Criteria:

Patients will not be enrolled if any of the following criteria apply:

- Prior chemotherapy for metastatic disease.
- History of prior malignancy in the last 10 years (other than non melanoma skin cancer or excised cervical carcinoma in situ).
- Radiation to disease areas within 3 weeks of study initiation.
- Symptomatic peripheral neuropathy > grade 2 according to the National Cancer Institute (NCI) Common Toxicity Criteria.
- Other serious illness or medical condition.
- LVEF < 50% as determined by echocardiogram or MUGA scan.
- Congestive hearth failure or angina pectoris even if it is medically controlled. Previous history of myocardial infarction within 1 year from study entry, uncontrolled high risk hypertension or arrhythmia.
- History of significant neurologic or psychiatric disorders including dementia or seizures.
- Active infection.
- Active peptic ulcer, unstable diabetes mellitus or other contraindications for the use of dexamethasone.
- Concurrent treatment with other experimental drugs. Participation in another clinical trial with any investigational drug within 30 days prior to study screening.
- Concurrent treatment with corticosteroids used for reasons other than for premedication. However patients receiving chronic treatment with corticosteroids (> 6 months) at low dose (< 20 mg of methylprednisolone or equivalent dose of other corticosteroids) for whichever reason are eligible.
- Taxane-based adjuvant or neo-adjuvant chemotherapy < 12 months.
- Other concurrent chemotherapy, immunotherapy, radiotherapy or any other investigational medication, for the treatment of the tumor.
- Pregnant or breast-feeding women.

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

No Contacts or Locations Provided

More Information

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00687440 History of Changes
Other Study ID Numbers:	P03679 Eudract No. 2004-003989-15
Study First Received:	May 27, 2008
Results First Received:	January 21, 2010
Last Updated:	October 29, 2014
Health Authority:	Italy: Ministry of Health

Additional relevant MeSH terms:

Breast Neoplasms	Antimitotic Agents
Breast Diseases	Antineoplastic Agents
Neoplasms	Enzyme Inhibitors
Neoplasms by Site	Mitosis Modulators
Skin Diseases	Molecular Mechanisms of Pharmacological Action
Docetaxel	Pharmacologic Actions
Doxorubicin	Therapeutic Uses
Liposomal doxorubicin	Topoisomerase II Inhibitors
Trastuzumab	Topoisomerase Inhibitors
Antibiotics, Antineoplastic	Tubulin Modulators

ClinicalTrials.gov processed this record on May 08, 2016

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Results First Received: January 21, 2010

Study Type:	Interventional
Study Design:	Endpoint Classification: Efficacy Study; Intervention Model: Single Group Assignment; Masking: Open Label; Primary Purpose: Treatment
Condition:	Breast Neoplasm
Interventions:	Drug: Pegylated Liposomal Doxorubicin Drug: Docetaxel Drug: Trastuzumab

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Caelyx, Docetaxel, Trastuzumab	Stage 1: subjects will receive Caelyx one day every 3 weeks in combination with docetaxel one day every 3 weeks and trastuzumab once weekly during 6 cycles. At the end of this stage, based on the number of cardiac events, subjects will proceed to a second stage or restart with a lower dose of Caelyx. Stage 2: subjects will be treated with the recommended dose of Caelyx (defined in the first stage) in combination with docetaxel and trastuzumab.

Participant Flow: Overall Study

	Caelyx, Docetaxel, Trastuzumab
STARTED	**27** [1]
COMPLETED	**15**
NOT COMPLETED	**12**
Adverse Event	**3**
Lost to Follow-up	**3**
Lack of Efficacy	**2**
Death	**2**
Not specified	**1**
Missing	**1**

[1] Number of screened participants

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Caelyx, Docetaxel, Trastuzumab	Stage 1: subjects will receive Caelyx one day every 3 weeks in combination with docetaxel one day every 3 weeks and trastuzumab once weekly during 6 cycles. At the end of this stage, based on the number of cardiac events, subjects will proceed to a second stage or restart with a lower dose of Caelyx. Stage 2: subjects will be treated with the recommended dose of Caelyx (defined in the first stage) in combination with docetaxel and trastuzumab.

Baseline Measures

	Caelyx, Docetaxel, Trastuzumab
Number of Participants [units: participants]	**27**

Age, Customized [units: years]	**27**
Gender [units: participants]	
Female	**27**
Male	**0**
Region of Enrollment [units: participants]	
Italy	**27**

Outcome Measures

1. Primary: Number of Participants Who Had a Tumor Response, According to Standard RECIST (Response Evaluation Criteria in Solid Tumors) Criteria [Time Frame: Week 09, Week 18, at the end of each patient's treatment, and at 3, 6, 9, and 12 months after end of treatment.]

Hide Outcome Measure 1

Measure Type	Primary
Measure Title	Number of Participants Who Had a Tumor Response, According to Standard RECIST (Response Evaluation Criteria in Solid Tumors) Criteria
Measure Description	Those who achieved either complete (disappearance of all target lesions) or partial (at least 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum LD) response.
Time Frame	Week 09, Week 18, at the end of each patient's treatment, and at 3, 6, 9, and 12 months after end of treatment.
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Intent-to-treat population

Reporting Groups

	Description
Caelyx, Docetaxel, Trastuzumab	Stage 1: subjects will receive Caelyx one day every 3 weeks in combination with docetaxel one day every 3 weeks and trastuzumab once weekly during 6 cycles. At the end of this stage, based on the number of cardiac events, subjects will proceed to a second stage or restart with a lower dose of Caelyx. Stage 2: subjects will be treated with the recommended dose of Caelyx (defined in the first stage) in combination with docetaxel and trastuzumab.

Measured Values

	Caelyx, Docetaxel, Trastuzumab
Number of Participants Analyzed [units: participants]	**26**
Number of Participants Who Had a Tumor Response, According to Standard RECIST (Response Evaluation Criteria in Solid Tumors) Criteria [units: Participants]	

Participants who had a complete tumor response	**2**
Participants who had a partial tumor response	**13**
Participants who did not have a tumor response	**11**

No statistical analysis provided for Number of Participants Who Had a Tumor Response, According to Standard RECIST (Response Evaluation Criteria in Solid Tumors) Criteria

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Reporting Groups

	Description
Caelyx, Docetaxel, Trastuzumab	No text entered.

Serious Adverse Events

	Caelyx, Docetaxel, Trastuzumab
Total, serious adverse events	
# participants affected / at risk	**6/27 (22.22%)**
Blood and lymphatic system disorders	
NEUTROPENIA † 1	
# participants affected / at risk	**1/27 (3.70%)**
# events	**1**
Gastrointestinal disorders	
STOMATITIS † 1	
# participants affected / at risk	**1/27 (3.70%)**
# events	**1**
VOMITING † 1	
# participants affected / at risk	**1/27 (3.70%)**
# events	**1**
General disorders	
MUCOSAL INFLAMMATION † 1	
# participants affected / at risk	**1/27 (3.70%)**
# events	**1**
PYREXIA † 1	
# participants affected / at risk	**1/27 (3.70%)**
# events	**1**

Infections and infestations	
SEPSIS † 1	
# participants affected / at risk	**1/27 (3.70%)**
# events	**1**
Investigations	
EJECTION FRACTION DECREASED † 1	
# participants affected / at risk	**1/27 (3.70%)**
# events	**1**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	
METASTASES TO MENINGES † 1	
# participants affected / at risk	**1/27 (3.70%)**
# events	**1**
Nervous system disorders	
COMA † 1	
# participants affected / at risk	**1/27 (3.70%)**
# events	**1**
Respiratory, thoracic and mediastinal disorders	
PULMONARY OEDEMA † 1	
# participants affected / at risk	**1/27 (3.70%)**
# events	**1**
Skin and subcutaneous tissue disorders	
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME † 1	
# participants affected / at risk	**2/27 (7.41%)**
# events	**2**
Vascular disorders	
HYPOTENSION † 1	
# participants affected / at risk	**1/27 (3.70%)**
# events	**1**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 9.1

Other Adverse Events

Hide Other Adverse Events

Time Frame	No text entered.
Additional Description	No text entered.

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Caelyx, Docetaxel, Trastuzumab	No text entered.

Other Adverse Events

	Caelyx, Docetaxel, Trastuzumab
Total, other (not including serious) adverse events	
# participants affected / at risk	**21/27 (77.78%)**
Blood and lymphatic system disorders	
LEUKOPENIA † 1	
# participants affected / at risk	**5/27 (18.52%)**
# events	**18**
LYMPHOPENIA † 1	
# participants affected / at risk	**2/27 (7.41%)**
# events	**10**
NEUTROPENIA † 1	
# participants affected / at risk	**5/27 (18.52%)**
# events	**10**
Gastrointestinal disorders	
ABDOMINAL PAIN † 1	
# participants affected / at risk	**3/27 (11.11%)**
# events	**8**
ABDOMINAL PAIN UPPER † 1	
# participants affected / at risk	**3/27 (11.11%)**
# events	**6**
CONSTIPATION † 1	
# participants affected / at risk	**3/27 (11.11%)**
# events	**5**
DIARRHOEA † 1	
# participants affected / at risk	**7/27 (25.93%)**
# events	**11**
GASTRITIS † 1	
# participants affected / at risk	**2/27 (7.41%)**
# events	**2**
NAUSEA † 1	
# participants affected / at risk	**8/27 (29.63%)**
# events	**9**
STOMATITIS † 1	
# participants affected / at risk	**7/27 (25.93%)**
# events	**28**
VOMITING † 1	
# participants affected / at risk	**3/27 (11.11%)**
# events	**3**

General disorders	
ASTHENIA † 1	
# participants affected / at risk	**8/27 (29.63%)**
# events	**10**
CHEST PAIN † 1	
# participants affected / at risk	**2/27 (7.41%)**
# events	**5**
FATIGUE † 1	
# participants affected / at risk	**2/27 (7.41%)**
# events	**3**
MUCOSAL INFLAMMATION † 1	
# participants affected / at risk	**6/27 (22.22%)**
# events	**22**
OEDEMA PERIPHERAL † 1	
# participants affected / at risk	**2/27 (7.41%)**
# events	**3**
PYREXIA † 1	
# participants affected / at risk	**6/27 (22.22%)**
# events	**7**
Nervous system disorders	
HEADACHE † 1	
# participants affected / at risk	**2/27 (7.41%)**
# events	**2**
PARAESTHESIA † 1	
# participants affected / at risk	**3/27 (11.11%)**
# events	**3**
Skin and subcutaneous tissue disorders	
ALOPECIA † 1	
# participants affected / at risk	**4/27 (14.81%)**
# events	**4**
NAIL DISORDER † 1	
# participants affected / at risk	**2/27 (7.41%)**
# events	**2**
ONYCHOLYSIS † 1	
# participants affected / at risk	**2/27 (7.41%)**
# events	**2**
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME † 1	
# participants affected / at risk	**16/27 (59.26%)**
# events	**43**
RASH † 1	
# participants affected / at risk	**3/27 (11.11%)**
# events	**4**

† Events were collected by systematic assessment

1 Term from vocabulary, MedDRA 9.1

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data
No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.
There is **NOT** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Results Point of Contact:

Name/Title: Senior Vice President, Global Clinical Development
Organization: Merck Sharp & Dohme Corp.
e-mail: ClinicalTrialsDisclosure@merck.com

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Health Authority:	Italy: Ministry of Health

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