Trial record **1 of 1** for: NCT03326674

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Tesetaxel Plus Reduced Dose of Capecitabine vs. Capecitabine in HER2 Negative, HR Positive, MBC (CONTESSA) (CONTESSA)

ClinicalTrials.gov Identifier: NCT03326674

Recruitment Status : Recruiting
First Posted : October 31, 2017
Last Update Posted : November 2, 2018

See **Contacts and Locations**

Sponsor:
Odonate Therapeutics, LLC

Information provided by (Responsible Party):
Odonate Therapeutics, LLC

Study Details | **Tabular View** | **No Results Posted** | Disclaimer | How to Read a Study Record

Study Description

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Brief Summary:

The primary objective is to compare the efficacy of tesetaxel plus a reduced dose of capecitabine versus the approved dose of capecitabine alone in patients with HER2 negative, HR positive LA/MBC previously treated with a taxane in the neoadjuvant or adjuvant setting.

Approximately 600 eligible patients will be randomly assigned in a 1:1 ratio to either Arm A (tesetaxel plus a reduced dose of capecitabine) or Arm B (approved dose of capecitabine alone).

Condition or disease	Intervention/treatment	Phase
Breast Cancer	Drug: Tesetaxel and Capecitabine Drug: Capecitabine	Phase 3

Detailed Description:

This is a multinational, multicenter, randomized, open-label, parallel group Phase 3 study. The primary objective is

to compare the efficacy of tesetaxel plus a reduced dose of capecitabine versus the approved dose of capecitabine alone based on PFS, as assessed by an Independent Radiologic Review Committee (IRC), in patients with HER2 negative, HR positive, LA/MBC previously treated with a taxane in the neoadjuvant or adjuvant setting.

Patients randomly assigned to Arm A (tesetaxel plus a reduced dose of capecitabine) will be administered:

- Tesetaxel (27 mg/m2) orally once every 21 days on Day 1 of each 21-day cycle; and
- Capecitabine (825 mg/m2) orally twice daily (in the morning and evening after a meal, for a total daily dose of 1,650 mg/m2) beginning with the evening dose on Day 1 through the morning dose on Day 15 of each 21-day cycle

Patients randomly assigned to Arm B (approved dose of capecitabine alone) will be administered:

• Capecitabine (1,250 mg/m2) orally twice daily (in the morning and evening after a meal, for a total daily dose of 2,500 mg/m2), beginning with the evening dose on Day 1 through the morning dose on Day 15 of each 21-day cycle Dose modifications for tesetaxel and/or capecitabine are described in the Study protocol.

Patients will be treated until documentation of progressive disease (PD), evidence of unacceptable toxicity, or other decision to discontinue treatment.

Study Design

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Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	600 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	Randomized, Phase 3 Study of Tesetaxel Plus a Reduced Dose of Capecitabine Versus Capecitabine Alone in Patients With HER2 Negative, HR Positive, Locally Advanced or Metastatic Breast Cancer Previously Treated With a Taxane
Actual Study Start Date :	December 21, 2017
Estimated Primary Completion Date :	September 2020
Estimated Study Completion Date :	March 2023

Resource links provided by the National Library of Medicine

Genetics Home Reference related topics:
Breast cancer

Drug Information available for: Capecitabine

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: Arm A: Tesetaxel and Capecitabine Tesetaxel (27 mg/m2) orally once every 21 days on Day 1 of each 21-day cycle; and Capecitabine (825 mg/m2) orally twice daily (in the morning and evening after a meal, for a total daily dose of 1,650 mg/m2) beginning with the evening dose on Day 1 through the morning dose on	Drug: Tesetaxel and Capecitabine Tesetaxel plus reduced dose of Capecitabine vs. approved dose of Capecitabine

Day 15 of each 21-day cycle	
Active Comparator: Arm B: Capecitabine Capecitabine (1,250 mg/m2) orally twice daily (in the morning and evening after a meal, for a total daily dose of 2,500 mg/m2) beginning with the evening dose on Day 1 through the morning dose on Day 15 of each 21-day cycle	Drug: Capecitabine Capecitabine alone at approved dose

Outcome Measures

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Primary Outcome Measures :

1. PFS [Time Frame: Approximately 2.5 - 3 years]

   Progression Free Survival

Secondary Outcome Measures :

1. OS [Time Frame: Approximately 5 - 5.5 years]

   Overall Survival

2. ORR [Time Frame: Approximately 2.5 - 3 years]

   Objective Response Rate

3. DCR [Time Frame: Approximately 2.5 - 3 years]

   Disease Control Rate

4. CNS ORR in patients with CNS metastases at Baseline [Time Frame: Approximately 2.5 -3 years]

   CNS Objective Response Rate as assessed by the CNS Independent Review Committee (IRC)

5. CNS PFS in patients with CNS metastases at Baseline or a history of CNS metastases in the intent-to-treat (ITT) population [Time Frame: Approximately 2.5 -3 years]

   CNS Progression Free Survival as assessed by the CNS IRC

6. CNS OS in patients with CNS metastases at Baseline or a history of CNS metastases [Time Frame: Approximately 2.5 -3 years]

   CNS Overall Survival as assessed by the CNS IRC

Other Outcome Measures:

1. PRO [Time Frame: Approximately 2.5 - 3 years]

   Patient Reported Outcomes - EORTC QLQ-C30 Global Health Status

2. Incidence of Treatment-Emergent Adverse Events as assessed by CTCAE v5.0 [Time Frame: Approximately 5 - 5.5 years]

   Adverse Events will be collected at each visit and at unscheduled visits, as clinically indicated

3. Incidence of clinical laboratory abnormalities as assessed by CBC, serum chemistry and coagulation testing [Time Frame: Approximately 5 - 5.5 years]

   Laboratory data will be collected at each visit, and unscheduled visits as appropriate

4. Peak plasma concentration (Cmax) of tesetaxel [Time Frame: [Approximately 2.5-3.0 years] Pre-dose and 0.5 hour post-dose on Day 1 of Cycle 1, 2 and 3 and anytime on Day 15 +/- 2 days of Cycle 1 and 2 (cycles are 21 days)]

   Maximum plasma concentration (Cmax) of tesetaxel

5. Area under the plasma concentration versus time curve (AUC) of tesetaxel [Time Frame: [Approximately 2.5-3.0 years] Pre-dose and 0.5 hour post-dose on Day 1 of Cycle 1, 2 and 3 and anytime on Day 15 +/- 2 days of Cycle 1 and 2 (cycles are 21 days)]

   Area under the curve (AUC) of tesetaxel

Eligibility Criteria

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Information from the National Library of Medicine

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, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Female or male patients at least 18 years of age
2. Histologically or cytologically confirmed breast cancer
3. HER2 negative disease based on local testing: American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines should be utilized for assessing HER2 status.
4. HR (ER and/or PgR) positive disease based on local testing: ASCO/CAP guidelines should be utilized for assessing HR status.
5. Measurable disease per RECIST 1.1 or bone-only disease with lytic component.
   - Patients with bone-only metastatic cancer must have a lytic or mixed lytic-blastic lesion that can be accurately assessed by computerized tomography (CT) or magnetic resonance imaging (MRI). Patients with bone-only disease without a lytic component (ie, blastic-only metastasis) are not eligible.
   - Known metastases to the central nervous system (CNS) are permitted but not required. The following criteria apply:
     - Patients must be neurologically stable and either off corticosteroids or currently treated with a

maximum daily dose of 4 mg of dexamethasone (or equivalent), with no increase in corticosteroid dose within 7 days prior to Randomization

- Patients with a history of CNS metastases but with no current evidence of CNS lesions following local therapy are eligible
- Patients may have CNS metastases that are stable or progressing radiologically
- Patients with current evidence of leptomeningeal disease are not eligible
- Patients may have untreated brain metastases or previously treated brain metastases, as long as no immediate local CNS-directed therapy is indicated
- Any prior whole brain radiation therapy must have been completed > 14 days prior to the date of Randomization
- Prior stereotactic brain radiosurgery is permitted
- CNS surgical resection must have been completed > 28 days prior to the date of Randomization; patient must have complete recovery from surgery

6. Eastern Cooperative Oncology Group (ECOG) performance status 0, 1, or 2
7. Prior therapy (at least one completed dose) with a taxane-containing regimen in the neoadjuvant or adjuvant setting
8. Prior therapy with an anthracycline-containing regimen in the neoadjuvant, adjuvant, or metastatic setting, where indicated by local regulation or Investigator judgment.
9. Prior endocrine therapy with or without a CDK 4/6 inhibitor unless endocrine therapy is not indicated (ie, short relapse-free interval while on adjuvant endocrine therapy [endocrine resistance]; rapidly progressing disease/visceral crisis; or endocrine intolerance). Any targeted therapies approved for HER2 negative, HR positive LA/MBC, including everolimus, are permitted as prior therapy. There is no limit to the number of prior endocrine therapies.
10. Documented disease recurrence or disease progression of: (a) locally advanced disease that is not considered curable by surgery and/or radiation; or (b) metastatic disease.
11. Adequate hematologic, hepatic, and renal function, as evidenced by:
    - Absolute neutrophil count (ANC) ≥ 1,500/μL without colony-stimulating factor support
    - Platelet count ≥ 100,000/μL
    - Hemoglobin ≥ 10 g/dL without need for hematopoietic growth factor or transfusion support
    - Total bilirubin < 1.5 × upper limit of normal (ULN); does not apply to patients with Gilbert's syndrome
    - Alanine aminotransferase (ALT) < 3 × ULN unless hepatic metastases are present, then < 5 × ULN
    - Aspartate aminotransferase (AST) < 3 × ULN unless hepatic metastases are present, then < 5 × ULN
    - Alkaline phosphatase < 2.5 × ULN unless hepatic metastases are present, then < 5 × ULN
    - Calculated creatinine clearance ≥ 50 mL/min
    - Serum albumin ≥ 3.0 g/dL
    - Prothrombin time (PT) < 1.5 × ULN or international normalized ratio (INR) < 1.3 and partial thromboplastin time (PTT) < 1.5 × ULN; unless the patient is on a therapeutic anticoagulant
12. Complete recovery to baseline or Grade 1 per National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 from adverse effects of prior surgery, radiotherapy, endocrine therapy, and other therapy, as applicable, with the exception of Grade 2 alopecia from prior chemotherapy
13. Ability to swallow an oral solid-dosage form of medication
14. A negative serum pregnancy test within 7 days prior to the first dose of Study treatment in women of childbearing potential (ie, all women except those who are post menopause for ≥ 1 year or who have a history of hysterectomy or surgical sterilization)
15. Women of childbearing potential must use an effective, non-hormonal form of contraception from Screening

throughout the Treatment Phase and until 70 days after the last dose of Study treatment

• Acceptable methods include: copper intrauterine device or double barrier methods, including male/female condoms with spermicide and use of contraceptive sponge, cervical cap, or diaphragm

16. Male patients must use an effective, non-hormonal form of contraception from Screening throughout the Treatment Phase and until 130 days after last dose of Study treatment

    • Acceptable methods include male/female condoms with spermicide, or vasectomy with medical confirmation of surgical success.

17. Written informed consent and authorization to use and disclose health information
18. Ability to comprehend and comply with the requirements of the Study

Exclusion Criteria:

1. Two or more prior chemotherapy regimens for advanced disease
2. Prior treatment with a taxane in the metastatic setting
3. Prior treatment with capecitabine at any dose
4. Current evidence of leptomeningeal disease
5. Other cancer that required therapy within the preceding 5 years other than adequately treated: (a) non-melanoma skin cancer or in situ cancer; or (b) following approval by the Medical Monitor, other cancer that has a very low risk of interfering with the safety or efficacy endpoints of the Study
6. Known human immunodeficiency virus infection, unless well controlled. Patients who are on an adequate antiviral regimen with no evidence of active infection are considered well controlled.
7. Active hepatitis B or active hepatitis C infection
8. Other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with Study participation or investigational product administration or may interfere with the interpretation of Study results and, in the judgment of the Investigator, would make the patient inappropriate for entry into this Study.
9. Presence of neuropathy > Grade 1 per NCI CTCAE version 5.0
10. History of hypersensitivity to taxanes; hypersensitivity to the solvent does not preclude patient participation in this Study
11. Anticancer treatment, including endocrine therapy, radiotherapy (except stereotactic brain surgery), chemotherapy, biologic therapy, or therapy in an investigational clinical study, ≤ 14 days prior to the date of Randomization
12. Major surgery ≤ 28 days prior to the date of Randomization; patient must have complete recovery from surgery
13. Less than 2 weeks or 5 plasma half-lives (whichever is greater) since last use of a medication or ingestion of an agent, beverage, or food that is a known clinically relevant strong inhibitor or known clinically relevant inducer of the cytochrome P450 (CYP) 3A pathway (patients should discontinue taking any regularly taken medication that is a strong inhibitor or inducer of the CYP3A pathway)
14. History of hypersensitivity or unexpected reactions to capecitabine, other fluoropyrimidine agents, or any of their ingredients
15. Known dihydropyrimidine dehydrogenase (DPD) deficiency. Testing for DPD deficiency must be performed where required by local regulations, using a validated method that is approved by local health authorities.
16. Pregnant or breastfeeding
17. If, in the opinion of the Investigator, the patient is deemed unwilling or unable to comply with the requirements of the Study
18. Treatment with brivudine, sorivudine, or its chemically-related analogs ≤ 28 days prior to the date of Randomization

Contacts and Locations

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Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT03326674***

Contacts

Contact: Valerie Legagneur 860-404-2271 vlegagneur@odonate.com

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Show 168 Study Locations

Sponsors and Collaborators

Odonate Therapeutics, LLC

Investigators

Study Director: Joseph O'Connell, MD Odonate Therapeutics, LLC

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Responsible Party: Odonate Therapeutics, LLC
ClinicalTrials.gov Identifier: NCT03326674 History of Changes
Other Study ID Numbers: ODO-TE-B301
First Posted: October 31, 2017 Key Record Dates
Last Update Posted: November 2, 2018
Last Verified: October 2018

Individual Participant Data (IPD) Sharing Statement:
Plan to Share IPD: Undecided
Plan Description: Currently under evaluation by the organization

Studies a U.S. FDA-regulated Drug Product: Yes
Studies a U.S. FDA-regulated Device Product: No

Keywords provided by Odonate Therapeutics, LLC:

Tesetaxel	Combination of tesetaxel and capecitabine
Capecitabine	Taxanes
HER2 negative	Metastatic breast cancer
Hormone Receptor positive	Breast cancer
Locally advanced or metastatic breast cancer	Central nervous system (CNS) metastases

Additional relevant MeSH terms:

Breast Neoplasms	Capecitabine
Neoplasms by Site	Antimetabolites, Antineoplastic
Neoplasms	Antimetabolites

Breast Diseases
Skin Diseases
Molecular Mechanisms of Pharmacological Action
Antineoplastic Agents