Clinical Trial Details (PDF Generation Date :- Fri, 27 Jan 2023 19:23:58 GMT)

CTRI Number	CTRI/2008/091/000017 [Registered on: 22/10/2008] -
Last Modified On	03/04/2013
Post Graduate Thesis	No
Type of Trial	Interventional
Type of Study	Drug Other (Specify) [Sorafenib 200mg/Matching placebo Tablets]
Study Design	Randomized, Parallel Group, Placebo Controlled Trial
Public Title of Study	A study to determine the safety and activity of Sorafenib in patients with locally recurrent or metastatic breast cancer
Scientific Title of Study	A Double-Blind, Randomized Phase 2b Study Evaluating the Efficacy and Safety of Sorafenib Compared to Placebo when Administered in Combination with Paclitaxel in Patients with Locally Recurrent or Metastatic Breast Cancer

Secondary IDs if Any

Secondary ID	Identifier
NCT00499525	ClinicalTrials.gov
NU07B1	Protocol Number

Details of Principal Investigator or overall Trial Coordinator (multi-center study)

Details of Principal Investigator	
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Source of Monetary or Material Support

Source of Monetary or Material Support
> Onyx Pharmaceuticals, Inc., (“Onyx”), USA 2100 Powell Street Emeryville, CA 94608

Primary Sponsor

Primary Sponsor Details	
Name	William J Gradishar Feinberg School of MedicineChicago Illinois USA
Address	Onyx Pharmaceuticals, 249, East Ground Avenue, South San Francisco CA 94608
Type of Sponsor	Pharmaceutical industry-Global

Details of Secondary Sponsor

Name	Address
NIL	NIL

Countries of Recruitment

List of Countries
India

Sites of Study

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
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Details of Ethics Committee

Name of Committee	Approval Status	Date of Approval	Is Independent Ethics Committee?
Apollo Specialty Hospital, #3, Globe Building(3rd Floor), Rathna Nagar, Teynampet, Chennai-600035	Approved	11/03/2008	No
CREC, Madhav Niwas,	Approved	06/12/2008	Yes

Opposite Octroi Naka, Hingna Road, Nagpur - 440019			
Dr. Kamakshi Memorial Hospital, No. 1, Radial Road, Pallikaranai, Chennai- 600091	Approved	06/03/2008	No
Ethics Committee - Director, Mahaveer Cancer Sansthan, Phulwari Sharif, Patna - 801 505, India	Approved	26/09/2008	No
Ethics Committee Apollo Hospital Educational & Research Foundation, Basement Hostel Complex, Indraprastha Apollo Hospitals, Sarita Vihar, NewDelhi-110076	Approved	14/03/2008	No
Ethics Committee, Jaslok Hospital & Research Centre, 15 , Dr. G.Deshmukh Marg, Mumbai -400 026.	Approved	22/05/2008	No
Ethics committee, Professor of Medical Oncology,Head Delhi Cancer Registry, Room no.- 401, Fourth Floor, Institute Rotary Cancer Hospital, AIIMS, NewDelhi- 110029	Approved	10/04/2008	No
Ethics Committee, Room 212A, Department of Medical Oncology,Sir Ganga Ram Hospital, Rajinder Nagar, New Delhi-110060.	Approved	03/06/2008	No
Ethics Committee, The Gujarat Cancer and Research Centre, Civil Hospital Campus, Asarwa, Ahmedabad-380016	Approved	13/08/2008	No
EthicsCommittee, Additional Professor, Breast Cancer Clinic, Regional cancer Center, Trivandrum 695011	Approved	27/06/2008	No
Heart Care Clinic, Hemato Oncology Clinic,Vedanta Institute of Medical sciences, Stadium to commerce College Road,	Approved	06/05/2008	No

Navrangpura. Ahmedabad, 380 009			
Institute Ethics Committee,Department of Medical OncologyThe Gujarat Cancer and Research Centre, Civil Hospital Campus, Asarwa, Ahmedabad-380016	Approved	13/08/2008	No
Institutional Ethics Committee, Department of Medical Oncology,Kasturba Medical College Hospital,Attavar,Mangalore-575001	Approved	16/10/2008	No
Institutional Ethics Committee, Jawaharlal Nehru Cancer Hospital and Research Centre, Idgah hills, Bhopal-1, M.P, 462 001 India	Approved	15/03/2008	No
Institutional Ethics Committee, Nizams Institute of Medical Sciences, Panjagutta, Hyderabad 500082.	Approved	15/05/2008	No
Kidwai Memorial Institute of Oncology,Dr .M.H.Merigowda Road, Bangalore 560029.	Approved	09/02/2008	No
Poona Medical Research Foundation, Medical Oncologist, New Cancer Building, Ruby Hall Clinic, 40 Sassoon Road,Pune-411001	Approved	18/03/2008	No
Shatabadi Super Speciality,Opp Mahamarg Bus Stand, Mumbai naka, Nashik 422005	Approved	16/02/2008	No
Sterling Hospital Ethics Committee, Memnagar, Ahmedabad, PIN-380052, India	Approved	01/05/2008	No
The Institutional Ethics Committee, Department of Medical Oncology, Amrita Institute of Medical Sciences, Elamakkara P.O., Kochi - 682026	Approved	20/10/2008	No

Regulatory Clearance Status from DCGI

Status	Date
Approved/Obtained	16/01/2008

Health Condition / Problems Studied

Health Type	Condition
Patients	Patients with locally recurrent or metastatic breast cancer

Intervention / Comparator Agent

Type	Name	Details
Intervention	Sorafenib	200 mg tablets
Comparator Agent	Placebo	Matching placebo tablets

Inclusion Criteria

Inclusion Criteria	
Age From	18.00 Year(s)
Age To	99.00 Year(s)
Gender	Female
Details	 Note: No upper age limit for this clinical trial, (indicated as 18 years and above) 1. Histologically or cytologically confirmed adenocarcinoma of the breast. 2. Measurable or evaluable locally recurrent or metastatic disease. (Locally recurrent disease must not be amenable to resection with curative intent.) All scans used to document measurable or evaluable disease must be done within 4 weeks prior to randomization. 3. Age greater than or equal to 18 years 4. Patients must not have had adjuvant or neoadjuvant taxane therapy within 12 months of randomization. 5. Patients must have discontinued other adjuvant chemotherapy at least 3 weeks prior to randomization. 6. Prior hormonal therapy for locally recurrent or metastatic disease is allowed. 7. Prior radiation therapy is allowed but must be completed at least 3 weeks prior to randomization. Previously radiated area(s) must not be the only site of disease. 8. ECOG Performance Status of 0 or 1 9. Adequate bone marrow, liver, and renal function as assessed by the following: - Hemoglobin greater than or equal to 9.0 g/dl - Absolute neutrophil count (ANC) greater than or equal to 1,500/mm3 - Platelet count greater than or equal to100,000/mm3 - Total bilirubin less than or equal to 2.0 times the upper limit of normal - ALT and AST less than or equal to 2.5 x upper limit of normal (less than or equal to 5 x upper limit of normal for patients with liver involvement) - International Normalized Ratio for Prothrombin Time (PT-INR) and activated partial prothrombin time (aPTT) less than or equal to 1.5 times the upper limit of normal for patients NOT on blood thinners. NOTE: Patients receiving anti-coagulation treatment with an agent such as warfarin or heparin will have a higher value but may be allowed to participate as long as the INR is measured prior to initiation of sorafenib/placebo and is monitored at least weekly, or as defined by the local standard of care, until INR is stable. - Creatinine less than or equal to 2.0 times the upper limit of normal 10. Women of childbearing potential must have a negative serum pregnancy test performed within 7 days prior to randomization and must agree to use adequate contraception prior to randomization and for the duration of study participation. 11. Patients must be able and willing to sign a written informed consent. A signed informed consent must be appropriately obtained prior to any study specific procedures. 12. Patients must be able to swallow and retain oral medication.

Exclusion Criteria

Exclusion Criteria	
Details	1. Patients with breast cancer over-expressing HER-2 (gene amplification by FISH or 3+ over-expression by immunohistochemistry). Patients with unknown HER-2 status are not eligible. 2. Patients with active brain metastases. Patients with neurological symptoms must undergo a contrast computed tomography (CT) scan or magnetic resonance imaging (MRI) of the

	brain to exclude active brain metastasis. Patients with treated brain metastases are eligible provided they have no evidence of brain disease and are off definitive therapy (including steroids) within 3 months prior to randomization. 3. Prior chemotherapy for locally recurrent or metastatic breast cancer 4. Major surgery, open biopsy, or significant traumatic injury within 4 weeks of randomization 5. Evidence or history of bleeding diathesis or coagulopathy 6. Serious, non-healing wound, ulcer, or bone fracture 7. Substance abuse, or medical, psychological, or social condition that may interfere with the patient?s participation in the study or evaluation of the study results 8. Pre-existing peripheral neuropathy ≥Grade 2 9. Use of cytochrome P450 enzyme-inducing anti-epileptic drugs (such as phenytoin, carbamazepine, or phenobarbital) 10. Clinically significant cardiac disease including congestive heart failure > class II NYHA (see Appendix IV), unstable angina (angina symptoms at rest) or new-onset angina (begun within the last 3 months), myocardial infarction within the past 6 months prior to randomization 11. Cardiac ventricular arrhythmias requiring anti-arrhythmic therapy and or uncontrolled hypertension (systolic blood pressure >150 mmHg or diastolic pressure >90 mmHg) despite optimal medical management 12. Thrombolic, embolic, venous, or arterial events such as a cerebrovascular accident including transient ischemic attacks within the past 6 months. No pulmonary hemorrhage/bleeding event > NCI-CTCAE Grade 2 within 4 weeks of randomization. No other hemorrhage/bleeding event greater than or equal to CTCAE Grade 3 within 4 weeks of randomization 13. Active clinically serious infection > NCI-CTCAE Grade 2 14. Known human immunodeficiency virus infection or chronic hepatitis B or C 15. Previous or concurrent cancer that is distinct in primary site or histology from breast cancer within 5 years prior to randomization EXCEPT cervical cancer in situ, treated basal cell carcinoma, superficial bladder tumors [Ta and Tis]. 16. Known or suspected allergy to sorafenib or hypersensitivity to paclitaxel or drugs using the vehicle Cremophor 17. Use of St. John?s Wort or rifampin (rifampicin) within 1 week of randomization 18. Prior treatment with bevacizumab or any other drugs (licensed or investigational) that target VEGF or VEGF-R 19. Concurrent anti-cancer therapy (chemotherapy, radiation therapy, surgery, immunotherapy, biologic therapy or tumor embolization) other than paclitaxel and sorafenib/placebo 20. Women that are pregnant or breast feeding 21. Use of any investigational drug within 30 days or 5 half-lives, whichever is longer, preceding randomization

Method of Generating Random Sequence	Stratified randomization
Method of Concealment	Centralized
Blinding/Masking	Participant, Investigator, Outcome Assessor and Date-entry Operator Blinded

Primary Outcome

Outcome	Timepoints
To compare progression free survival (PFS) in patients with sorafenib and paclitaxel versus patients treated with placebo and paclitaxel as a first-line therapy for locally recurrent or metastatic breast cancer	Events projected to occur November 2008

Secondary Outcome

Outcome	Timepoints
1. To compare the objective response rate, duration of response, time to progression, and survival of patients treated with sorafenib and paclitaxel versus placebo and paclitaxel. 2. To compare the safety of patients treated with sorafenib and paclitaxel versus placebo and	Overall survival events projected to occur August 2010

	paclitaxel
Target Sample Size	**Total Sample Size=**220 **Sample Size from India=**170 **Final Enrollment numbers achieved (Total)=** **Final Enrollment numbers achieved (India)=**
Phase of Trial	Phase 2
Date of First Enrollment (India)	05/05/2008
Date of First Enrollment (Global)	10/03/2008
Estimated Duration of Trial	**Years=**4 **Months=**0 **Days=**0
Recruitment Status of Trial (Global)	Completed
Recruitment Status of Trial (India)	Completed
Publication Details	
Brief Summary	It is a global multicenter trial. USA is the only other participating country other than India. Approvals are already in place from the concerned regulatory authorities including India. The study was filed under US IND. The US FDA after reviewing the IND submitted for this study concluded that the trial meets all the requirements for the exemptions from the IND regulations. Approval from US FDA with respect to exemption from the IND regulation (21 CFR § 312.2) for the referenced study is provided. A total of 220 patients will be randomly assigned (1:1 ratio) to receive either sorafenib and paclitaxel or placebo and paclitaxel. The trial is currently recruiting patients across 33 sites participating in the study from USA. Sponsor proposes to enroll 170 patients from India from up to 20 participating sites. A double-blind, randomized, Phase 2b trial in approximately 220 patients (greater than or equal to 18 years of age) with locally recurrent or metastatic breast cancer. The study will consist of a screening period, a treatment period, and a follow-up period. Screening Period Treatment Period Patients will be randomly assigned in a 1:1 ratio to sorafenib and paclitaxel or placebo and paclitaxel. During the randomization process, patients will be stratified by site of metastatic disease: visceral disease versus nonvisceral (osseous or soft tissue) disease. Randomization will be performed using a web-based randomization and product inventory control system (RPIC) provided by a third-party vendor. Follow-up Period Patients will enter the follow-up period upon documentation of disease progression, extraordinary medical circumstances, intolerable toxicities, or withdrawal of consent. Every reasonable effort should be taken to encourage patients to continue to be followed for evidence of disease progression even after study treatment discontinuation for reasons other than progressive disease. All patients will be followed for survival until the planned number of events for survival (120 deaths) has been reached. Assessment of survival will be performed approximately every 4 months. Duration of Treatment: Patients will receive study treatment until disease progression is documented, extraordinary medical circumstances occur, intolerable toxicities occur, or the patient withdraws consent. The primary objective is to compare progression free survival (PFS) in patients with sorafenib and paclitaxel versus patients treated with placebo and paclitaxel as a first-line therapy for locally recurrent or metastatic breast cancer The secondary objectives are: 1. To compare the objective response rate, duration of response, time to progression, and survival of patients treated with sorafenib and paclitaxel versus placebo and paclitaxel. 2. To compare the safety of patients treated with sorafenib and paclitaxel versus placebo and paclitaxel