Title: SWOG S0800: A Randomized Phase II Trial of Weekly Nanoparticle Albumin Bound Paclitaxel (NAB-Paclitaxel) (NSC-736631) With or Without Bevacizumab, Either Preceded by or Followed By Q 2 Week Doxorubicin (A) and Cyclophosphamide (C) Plus Pegfilgrastim (PEG-G) As Neoadjuvant Therapy for Inflammatory and Locally Advanced Her-2/Neu Negative Breast Cancer

Purpose: To compare two different treatment regimens for breast cancer prior to surgery to determine which regimen works better and to compare the type and severity of the side effects of each of the two treatment regimens.

Eligibility: Women with confirmed diagnosis of HER-2 negative inflammatory breast carcinoma and must not have received any prior treatment within the past five years.

Principal Investigator: Gorbaty, Mayer

Phase: II

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Approved Enrollment Number: 10

Current Enrollment: 5
Title: N093B: Phase I/II Study of Panobinostat (LBH589) and Letrozole in Patients with Triple Negative Metastatic Breast Cancer.

Purpose: To test the safety of the investigational drug LBH589 (panobinostat) when it is given with a set dose of letrozole. To find out what effects good and/or bad, LBH589 and letrozole have on men and women with metastatic breast cancer.

Eligibility: - Men and women equal to or greater than 18 years of age.
- Histologic proof of metastatic breast cancer that is unresected at registration (with no intention of resecting tumors during this study). Evidence of metastatic breast cancer confirmed by radiological imaging.
- Phase I Study: Measurable or non-measurable disease allowed.
- Phase II Study: Measurable disease.
- Both Phase I and Phase II: Metastatic site(s) must be amenable to biopsy.

- Post-menopausal according to any one of the following criteria:
  - Age ≥60 years old
  - Age ≥45 years old with last menstrual period ≥12 months prior to registration and estradiol and follicle-stimulating hormone (FSH) levels in postmenopausal range (per institutional normal limits)
  - Bilateral oophorectomy

- Tumor estrogen, progesterone and HER2 [tested by IHC or FISH (fluorescent in situhybridization)] status from the metastatic site. If not available, the results from the original tumor diagnosing the primary breast cancer may be used.
  - Phase I Study: Any ER, PR, or HER2 level acceptable, positive or negative.
  - Phase II Study: Triple negative disease only [ER- (defined as ≤1% by IHC), PR- (defined as ≤1% by IHC), and HER2-] Patients with triple negative breast cancer are allowed if there is clinical or radiographic evidence of tumor progression in the adjuvant or metastatic setting.

NOTE: If HER2 result by IHC is 2+ (equivocal), the tumor must be confirmed to be HER2- by FISH.
- Phase II only Prior treatments allowed:
  0 or 1 prior chemotherapy regimens for breast cancer
  ≤2 prior aromatase inhibitor regimens (including letrozole)

- The following laboratory values obtained □14 days prior to registration:
  - ANC >1500/mm³
  - Platelet count >100,000/mm³
  - Total bilirubin □ upper limit of normal (ULN)
  - SGPT (ALT) <3 x ULN or
    SGPT (ALT) ≤5 x ULN if elevations are due to liver metastases
  - SGOT (AST) <3 x ULN or
    SGOT (AST) ≤5 x ULN if elevations are due to liver metastases
• Serum creatinine <1.5 x ULN
• TSH <ULN

NOTE: Euthyroid patients are permitted to receive thyroid hormone supplements to treat their underlying hypothyroidism, as long as TSH is within normal limits.

ECOG Performance Status (PS). (This form is available on the NCCTG web site https://ncctg.mayo.edu/ncctg/forms/NonProtocolSpecificForms.)
- Phase I only: PS must be 0 or 1.
- Phase II only: Performance Status must be 0, 1 or 2.
- Ability to provide informed written consent.
- Willingness to return to Mayo Clinic (Phase I) or NCCTG enrolling institution (Phase II) for follow-up.
- Life expectancy >12 weeks.
- Willing to provide tissue samples for correlative research purposes (see Sections 4.0, 6.25, and 17.1).

Exclusion Criteria
- Known standard therapy for the patient’s disease that is potentially curative or definitely capable of extending life expectancy.
- Phase II only
  >1 prior chemotherapy regimen for breast cancer
  >2 prior aromatase inhibitor regimens
  - Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements.
  - Any of the following:
    • Chemotherapy <4 weeks prior to registration
    • Radiation therapy <4 weeks prior to registration
    • Radiation to >25% of bone marrow
  - Failure to fully recover from acute or reversible effects of prior chemotherapy regardless of interval since last treatment.
  - New York Heart Association (NYHA) Classification III or IV cardiovascular disease. (This form is available the NCCTG web site https://ncctg.mayo.edu/ncctg/forms/NonProtocolSpecificForms.)
  - Known CNS metastasis or seizure disorder.
  - Any of the following because this study involves an investigational agent whose genotoxic, mutagenic and teratogenic effects on the developing fetus and newborn are unknown.
    • Pregnant women
    • Nursing women
    • Men of childbearing potential who are unwilling to employ adequate contraception (as determined by the treating physician)
- Currently receiving treatment in a different clinical study in which investigational procedures are performed or investigational therapies are administered (utilized for a non-FDA-approved indication and in the context of a research investigation).
- Co-morbid systemic illnesses or other severe concurrent disease which, in the judgment of the investigator, would make the patient inappropriate for entry into this study or interfere significantly with the proper assessment of safety and toxicity of the prescribed regimens.
- Immunocompromised patients (other than that related to the use of corticosteroids) including patients known to be HIV positive.
- Receiving any other investigational agent concurrently which would be considered as a treatment for the primary neoplasm.
- History of other malignancy ≤5 years with the exception of non-melanoma skin cancer of carcinoma in-situ of the cervix.
- History of myocardial infarction ≤6 months, or congestive heart failure requiring use of ongoing maintenance therapy for life-threatening ventricular arrhythmias.
- Receiving CYP3A4 inhibitors and inducers or any other contraindicated agent.
- Congenital long QT syndrome or QTcF>450 msec on screening ECG:
  • Complete left bundle block or use of a permanent cardiac pacemaker, history or presence of ventricular tachyarrhythmias, clinically significant resting bradycardia (<50 beats per minute).
  • Right bundle branch block + left anterior hemiblock (bifascicular block).

**Principal Investigator:** Gorbaty, Mayer  
**Phase:** I/II  
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**Approved Enrollment Number:** 10  
**Current Enrollment:** 0
Title: S0927, A Randomized Placebo-Controlled Trial of Omega-3-Fatty Acid for the Control of Aromatase Inhibitor-Induced Musculoskeletal Pain and Stiffness in Women with Early Stage Breast Cancer, Phase III.

Purpose: To compare the effects, good and/or bad, of the nutritional supplement omega-3-fatty acid against placebo (contains no active ingredient) on the joint pain and stiffness that is associated with taking aromatase inhibitors.

Eligibility: -Patients must be women with histologically confirmed primary invasive adenocarcinoma of the breast (Stage I, II or III) with no evidence of metastatic disease.
-Patients must have undergone modified radical mastectomy or breast sparing surgery.
-Patients must have recovered from all side-effects of the surgery.
-Patients must be post-menopausal, as defined by at least one of the following:
a. ≥ 12 months since the last menstrual period OR
b. prior bilateral oophorectomy OR
c. previous hysterectomy with one or both ovaries left in place (or previous hysterectomy in which documentation of bilateral oophorectomy is unavailable) AND FSH values consistent with the institutional normal values for the post menopausal state. FSH levels must be obtained within 28 days prior to registration.
-Patients must be positive for either estrogen receptor (ER) and/or progesterone receptor (PgR) as determined by institutional standard.
-Patients must currently be taking a third-generation aromatase inhibitor (AI) -anastrozole (Arimidex®), letrozole (Femara®), or exemestane (Aromasin®) for at least the previous 90 days prior to registration with plans to continue for at least an additional 180 days after registration.
-Patients must have completed the S0927 Brief Pain Inventory-Short Form within 14 days prior to registration.
-Patients must have a worst pain/stiffness of at least 5 on the Brief Pain Inventory (item #2). The pain/stiffness must have started or increased since starting AI therapy.
-Patients must have a Zubrod performance status of 0 to 2.
-Patients must not have taken omega-3-fatty acid supplements within the past 3 months prior to registration and must agree to refrain from use of omega-3-fatty acid supplements from sources outside of this study.
-Patients must be willing to submit blood for serum free estradiol, total estradiol, serum inflammatory markers (IL6, TNF-α, CRP), DHA and EPA, lipid profile (LDL, HDL, triglycerides), DNA analysis (CYP19A1) and to submit urine for markers of joint degradation (CTX-II), and must be given the option to consent for specimen submission for banking and future translational medicine studies as outlined in Section 15.0. Baseline samples must be obtained prior to beginning treatment.
-Patients must be able to complete study questionnaires in English.
-Individuals must not have participated in a clinical trial with an investigational agent within 28 days prior to registration.
-Patients must not be on anticoagulation medication (i.e., heparin/warfarin) because of increased risk of bleeding within 28 days prior to registration.
-Patients must not have a history of bone fracture or surgery of the afflicted knees and/or hands within 6 months prior to registration.
-Patients must not be on narcotics within 14 days of registration.
-Patients may have received corticosteroid treatment however the following criteria apply:
a. Patients must not have received oral corticosteroids within the 28 days prior to registration.
b. Patients must not have received intramuscular corticosteroids within 28 days prior to registration.
c. Patients must not have received intra-articular steroids to the study joint within 28 days prior to registration.
d. Patients must not have received intra-articular steroids to any other joint within 28 days prior to registration.

- Patients must not have received topical analgesics (e.g., capsaicin preparations) to the study joint or any other analgesics (e.g., opiates, tramadol; with the exception of NSAIDs and acetaminophen) within 14 days prior to registration.
- No prior malignancy is allowed except for adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, DCIS, adequately treated Stage I or II cancer from which the patient is currently in complete remission, or any other cancer from which the patient has been disease-free for 5 years.
- All participants must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.
- At the time of patient registration, the treating institution's name and ID number must be provided to the Data Operations Center in Seattle in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the database.

Principal Investigator: Gorbaty, Mayer
Phase: III
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Approved Enrollment Number: 15
Current Enrollment: 0
Title: A Phase III, Randomized Clinical Trial of Standard Adjuvant Endocrine Therapy +/- Chemotherapy in Patients with 1-3 Positive Nodes, Hormone Receptor-Positive and Her2-Negative Breast Cancer with Recurrence Score (RS) of 25 or Less. (S1007)

Purpose: To find out if the oncotype DX® Recurrence Score can help decide whether patients should receive chemotherapy or not.

Eligibility: Patients must have a histologically confirmed diagnosis of node positive (1-3 nodes) invasive breast carcinoma with positive estrogen and/or progesterone receptor status, and negative HER-2, as determined by IHC or non-amplified FISH for screening. Estrogen and progesterone positivity must be assessed according to ASCO/CAP guidelines (assays are considered positive if there are at least 1% positive tumor nuclei in the sample on testing in the presence of expected reactivity of internal [normal epithelial elements] and external controls). If HER2 IHC is 2+, FISH must be performed and must not be positive (must be a ratio of = 2.2), but otherwise FISH is not required if IHC is 0 or 1+ by institutional standards.

- Patients with FISH in the indeterminate range (a ratio of 1.8 to 2.2) are eligible for the study only if they are not planning to receive treatment with trastuzumab.
- Patients will have undergone axillary staging by sentinel node biopsy or axillary lymph node dissection (ALND). Patients must have at least one, but no more than three known positive lymph nodes (pN1mi, pN1a, pN1b or pN1c), see Section 4.0 for definitions. Axillary node evaluation is to be performed per the standard of care at each institution.
- Patients must not have inflammatory breast cancer and must not have metastatic disease. Patients with a prior diagnosis of DCIS are eligible if they received mastectomy alone (no therapeutic radiation or endocrine therapy).
- Patients must have had either breast-conserving surgery with planned radiation therapy or total mastectomy (with or without planned postmastectomy radiation). Patients must have clear margins.
- Patients must be females ≥ 18 years of age. As the Oncotype DX® Recurrence Score has not been validated in men with breast cancer, men are not eligible for this study.
- Patients must have a performance status of 0-2 by Zubrod criteria
- Patients must not have begun chemotherapy or endocrine therapy for their breast cancer prior to registration.
- Patients must not require chronic treatment with systemic steroids or other immunosuppressive agents.
- Patients must not have received preventive tamoxifen or raloxifene, or have received prior therapeutic breast radiation.
- Pregnant or nursing women are not eligible because of the risk of fetal harm. Nursing women may participate only if nursing is discontinued, due to the possibility of harm to nursing infants from this treatment regimen. Women of reproductive potential who are sexually active must agree to use an effective non-hormonal contraceptive method while on treatment and for at least 3 months after completion of protocol treatment.
- No other prior malignancy is allowed except for the following: adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, adequately treated Stage 0, I or II cancer from which the patient is currently in complete remission, or any other cancer from which the patient has been disease-free for 5 years.
- Patients who are able to complete a questionnaire in English must be offered the opportunity to participate in the Quality of Life and Economic Substudy. Patients who are not able to complete a questionnaire in English are registered to S1007 without participating in the Quality of Life and Economic Substudy.

* Patients who consent to participate in the Quality of Life and Economic Substudy and who do not yet know the results of...
their Oncotype DX® screening must have completed the S1007 Health-Related Quality of Life Questionnaire: Enrollment form within 14 days prior to Step 1 Registration.

- Patients who consent to participate in the Quality of Life and Economic Substudy and who do already know their Oncotype DX® Recurrence Score (and it is 25 or less) will proceed to Step 2 Registration without completing the S1007 Health-Related Quality of Life Questionnaire Enrollment form (but will complete the S1007 Health-Related Quality of Life Questionnaire: Randomized Study form as outlined in Section 5.19).

Principal Investigator: Didolkar, Mukund S.

Phase: III

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Approved Enrollment Number: 15

Current Enrollment: 0
Title: A Randomized Phase III Trial of the Value of Early Local Therapy for the Intact Primary Tumor in Patients with Metastatic Breast Cancer (E2108)

Purpose: To compare the good and bad effects of a new approach that includes surgery plus radiation for the tumor in the breast to the standard approach of continued treatment with the medication which is working to control the tumor.

Eligibility: Patients (male or female) must have an intact primary (not recurrent) invasive carcinoma of the breast. Biopsy confirmation of the primary tumor should be by needle biopsy (preferred); incisional surgical biopsy is allowed as long as there is residual palpable or imageable tumor in the breast.
- Patients with synchronous contralateral breast cancer are excluded.
- Patients should have at least one site of distant metastatic disease. If only a single metastatic lesion is present, biopsy is mandatory.
- Radiology reports documenting status of disease prior to initiation of systemic therapy must be available. Scans must have been completed within 4 weeks prior to start of systemic therapy.
- If patient has only one site of metastatic disease, this must be proven by biopsy and the pathology report confirming the diagnosis of primary breast cancer, as well as the metastatic site, must be available.
- Patients may have had prior non-invasive (DCIS) cancer if there has been no recurrence.
- Patients with a history of other primary cancers are eligible if the pathology report confirming the diagnosis of primary breast cancer is available and the other primary cancer was curatively treated with a 5-year disease-free interval.
- Women of childbearing potential and sexually active males must be strongly advised to use an accepted and effective method of contraception.
- Patients with CNS metastases are eligible (as long as projected survival is > 6 months).
- Patients must have completed at least 16 weeks of optimal systemic therapy (appropriate to the tumor biological profile and the patient’s age and menopausal status), during which no more than 2 weeks of unscheduled dose interruption occurred for any reason. Rest weeks that are part of the schedule for treatment administration are included when calculating the duration of therapy.
- Documentation regarding the details of administration of all systemic chemotherapy must be available.
- Patients must not have experienced disease progression since the start of systemic therapy, as evidenced by radiographic documentation of disease status before treatment and within 2 weeks prior to randomization, including:
  a. No new sites of disease
  b. No enlargement of existing sites by 20% or more in longest diameter
  c. No symptomatic deterioration
- Patients must be judged to be candidates for complete resection with free margins followed by radiation therapy.
- Local disease at the primary site must be asymptomatic (no skin nodules or skin invasion, no ulceration, and no chest wall fixation).
Patients must have adequate organ function < 2 weeks prior to randomization, as measured by:

- Absolute neutrophil count > 1000/mm³
- Platelet count > 100,000/mm³
- Total bilirubin < 1.5 mg/dL
- AST < 2 X upper limit of normal
- Serum creatinine < 1.5 mg/dL

Principal Investigator: Gorbaty, Mayer

Phase: III

For more information, contact: Hagy, Melissa

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Approved Enrollment Number: 880

Current Enrollment: 0
Title: NSABP B-47: A Randomized Phase III Trial of Adjuvant Therapy Comparing Chemotherapy Alone (Six Cycles of Docetaxel Plus Cyclophosphamide or Four Cycles of Doxorubicin Plus Cyclophosphamide Followed by Weekly Paclitaxel) to Chemotherapy Plus Trastuzumab in Women with Node-Positive or High-Risk Node-Negative HER2-Low Invasive Breast Cancer

Purpose: To learn if adding a targeted therapy, trastuzumab (Herceptin®), to standard treatment with chemotherapy for early stage, HER2-low breast cancer, will prevent breast cancer from returning.

Eligibility: The patient must be female greater than 18 years old to be eligible. The patient must have an ECOG performance status of 0 or 1 (see Appendix A).

Patients with one or more of the following conditions are NOT eligible for this study:
- Primary tumor with any of the following HER2 testing results:
  - IHC staining intensity:
    - 0 on all evaluations of specimens
    - 3+ on evaluation of any specimen
  - ISH with a ratio of HER2 to CEP17 > 2.0 on evaluation of any specimen
  - ISH result indicating HER2 gene copy number > 4 per nucleus on evaluation of any specimen.
- T4 tumors including inflammatory breast cancer.
- Definitive clinical or radiologic evidence of metastatic disease. (Note: Chest imaging [mandatory for all patients] and other imaging [if required] must have been performed within 90 days prior to randomization.)

Principal Investigator: Gorbaty, Mayer

Phase: III

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Approved Enrollment Number: 20

Current Enrollment: 0
Title: A Phase 2 Study of BMS-754807 combined with Letrozole or BMS-754807 alone in Hormone-Receptor Positive Breast Cancer Subjects with Acquired Resistance to Non-Steroidal Aromatase Inhibitors (CA191-011)

Purpose: To assess the effect of oral doses of BMS-754807 alone or in combination with letrozole on breast cancer in order to determine, Preliminary effectiveness, Safety, Tolerability, and action of the drug in the body.

Eligibility: Inclusion Criteria

-Postmenopausal women ≥ 18 years of age with histologically confirmed HR+ (ER+ and/or PgR+) and HER-2 negative breast cancer according to IHC and measured by local lab standards

-Failed non-steroidal aromatase inhibitor treatment defined as locally advanced or metastatic breast cancer that has progressed:
  i) During or within 6 months after completion of adjuvant non-steroidal aromatase inhibitor treatment (as single agent or part of sequencing/ extended treatment with/ after tamoxifen), or
  ii) During non-steroidal aromatase inhibitor treatment in locally-advanced or metastatic setting

-Measurable disease by RECIST (v1.1) criteria (Appendix 1) or non-measurable disease that is clinically evaluable or with confirmatory documentation on CT or MRI of bone only disease

-A tumor paraffin tissue block or 10 - 20 unstained slides from the original diagnostic tumor specimen cut within one week of shipment

Note: Sites must confirm the availability of original tumor specimen before starting study medication administration; however, slides may be provided after study medication administration has been initiated

-Life expectancy of at least 3 months

-Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 (Appendix 2)

-Able to comply with visits and procedures required by the protocol

-Able to undergo biopsy at baseline and on treatment.

-Biopsy may be of chest wall, breast, skin, soft tissue, liver, or other site felt to be reasonably accessible in the opinion of the patient’s treating oncologist and physician performing the procedure

-If a biopsy requires general anesthesia, then it is only allowed if acquisition of tissue is necessary for clinical reasons (ie, is clinically indicated), and excess tissue that would otherwise have been discarded is then used for research purposes. If a biopsy requires general anesthesia, then a biopsy of that site for research purposes only, without a coexisting clinical indication is not allowed on this protocol

-If a biopsy requires general anesthesia, then it is only allowed if acquisition of tissue is necessary for clinical reasons (ie, is clinically indicated), and excess tissue that would otherwise have been discarded is then used for research purposes. If a biopsy requires general anesthesia, then a biopsy of that site for research purposes only, without a coexisting clinical indication is not allowed on this protocol

-Patients who undergo a research biopsy procedure for the purpose of this protocol, and in whom inadequate tissue is obtained, are still eligible and are not required to undergo a repeat biopsy in order to enter the study
v) Some patients may have had a clinically indicated biopsy upon recent disease progression and agreed to submit tissue to their institution’s tumor bank. If the tissue was processed as specified in this protocol, no additional pre-treatment biopsy is required as that specimen can be used for the purposes of participation in this clinical trial.

vi) For subjects with non-measurable bone only disease, biopsy may be waived at Investigator's discretion if procedure is determined to be hazardous to subjects well-being.

-Age and Reproductive Status

a) Women who are not of childbearing potential (ie, who are postmenopausal or surgically sterile; see Section 3.3.3 for the definition of WOCBP)

b) Women must not be breastfeeding

-Previous Treatment

a) Prior anti-cancer treatments are permitted (ie chemotherapy, radiotherapy, hormonal, or immunotherapy)

i) No more than 1 line of completed chemotherapy for locally-advanced or metastatic disease.

ii) Subjects are allowed to have failed multiple lines of hormonal treatment (antiestrogen, non-steroidal aromatase inhibitors) in adjuvant, locally-advanced or metastatic setting

iii) Prior therapy with tamoxifen is permitted but not required.

b) Toxicity related to prior anti-cancer therapy and/or surgery must either have resolved, returned to baseline or been deemed irreversible (except alopecia). Four (4) weeks must have elapsed between surgery and/or last dose of prior anti-cancer therapy and the initiation of study therapy, except for subjects who are on letrozole before study entry.

c) Prior to initiation of treatment (within 4 weeks) or during study participation, radiation therapy is allowed to a limited field (eg painful bone metastasis, painful lumps), if it is not the sole site of measurable and/or evaluable disease. Note: The Medical Monitor must be consulted prior to the administration of radiation therapy for subjects receiving treatment.

Exclusion Criteria

1) Sex and Reproductive Status

a) Women of childbearing potential (ie, who are not postmenopausal or surgically sterile; see Section 3.3.3 for the definition of WOCBP).

Note: Premenopausal women undergoing ovarian suppression are not eligible.

b) Men diagnosed with breast cancer

-Target Disease Exceptions

a) Subjects with known symptomatic brain metastasis. Subjects with controlled brain metastasis (no radiographic progression following radiation and/or surgical treatment, no neurological signs or symptoms and no maintenance therapy with steroids) will be allowed. Subjects with signs or symptoms suggestive of brain metastasis are not eligible unless brain metastases are ruled out by CT or MRL. Subjects with leptomeningeal disease are not eligible

b) Any condition requiring chronic use of steroids. Inhalation steroids for mild pulmonary disease not leading to exclusion based on other criteria (eg performance status) are allowed.

-Medical History and Concurrent Diseases
a) A serious uncontrolled medical disorder or active infection, which would impair the ability of the subject to receive protocol therapy
b) Any disorder with dysregulation of glucose homeostasis including but not limited to history of Type 1 or 2 Diabetes Mellitus, but excluding prior hyperglycemia in pregnancy
c) History of glucose intolerance or conditions with an ancillary effect on glucose, such as Cushing syndrome, pheochromocytoma, acromegaly, aldosteronism, or hyperthyroidism (except hyperthyroidism that is treated and adequately controlled for ≥ 4 weeks before entering the study)
d) Current or recent (within 3 months) gastrointestinal disease that could impact the absorption of study drug (e.g., unmanageable diarrhea or malabsorption at the time of screening)
e) Any gastrointestinal surgery that could impact the absorption of study drug
f) Any major surgery within 4 weeks of study drug administration
g) Inability to swallow oral medication
h) Inability to be venipunctured and/or tolerate venous access
i) Uncontrolled or significant cardiovascular disease including:
   i) Myocardial infarction, uncontrolled angina or, congestive heart failure within 6 months of screening
   ii) Left ventricular ejection fraction < the institutional lower limit of normal by echocardiogram or multigated acquisition (MUGA)
   iii) Diagnosed or suspected congenital long QT syndrome
   iv) Any history of clinically significant ventricular arrhythmias (such as ventricular tachycardia, ventricular fibrillation, or Torsade de Pointes). Controlled atrial fibrillation is not an exclusionary criterion
j) Subject with concomitant second malignancies (except adequately treated nonmelanoma skin cancers, in-situ carcinoma of the cervix and bladder) are excluded unless a complete remission was achieved at least 5 years prior to study entry and no additional therapy is required or anticipated to be required during the study period
k) Any other sound medical psychiatric and/or social reason as determined by the Investigator.

-Physical and Laboratory Test Findings
a) Fasting plasma glucose (FPG) levels indicating diabetes defined as fasting glucose ≥ 7.0 mmol/L (126 mg/dL)
   Note: A one-time retest may be allowed during the screening period as determined by the Investigator for subjects with FPG ≥ 7.0 mmol/L (≥ 126 mg/dL). Such cases should be discussed with the Sponsor prior to retesting the FPG.
b) Inadequate bone marrow function defined as:
   i) Absolute neutrophil count < 1,500 cells/mm³
   ii) Platelet count < 100,000 cells/mm³
   iii) Hemoglobin < 9.0 g/dL (5.6 mmol/L).
c) Inadequate hepatic function defined as:
   i) Alanine transaminase (ALT) and aspartate transaminase (AST) > 2.5 times the institutional upper limit of normal (IULN) (or > 5X IULN for subjects with liver metastasis)
   ii) Total bilirubin > 1.5 times the IULN (or > 2.5X IULN for subjects with liver metastasis)
d) Inadequate renal function defined as serum creatinine > 1.5 times the IULN
e) Abnormalities in serum sodium, potassium, calcium and magnesium levels ≥ Grade II at the time of enrollment (CTCAE Version 4.0, dated 14-Jun-10) Note: a one-time re-test may be allowed during the screening period as determined by the Investigator after appropriate electrolyte management. Such cases should be discussed with the Sponsor prior to re-testing.

-Allergies and Adverse Drug Reaction
a) History of allergy to compounds chemically related to BMS-754807
b) History of allergy to letrozole or compounds chemically related to letrozole
c) History of any significant drug allergy (such as anaphylaxis or hepatotoxicity).

-Prohibited Treatments and/or Therapies
a) Prior exposure to BMS-754807
b) Prior treatment with any anti-IGF-1R and/or IR biologic or small molecule
c) Exposure to any investigational drug within 4 weeks of study drug administration
d) More than 1 prior chemotherapy regimen for locally-advanced or metastatic disease (prior adjuvant or neoadjuvant chemotherapy does not count towards number of regimens in the locally-advanced or metastatic disease)
e) Drugs or interventions that are generally accepted to have a risk of causing Torsades de Pointes are prohibited. Subjects must have a wash-out period of at least 5 days or at least 5 half-lives of the drug (whichever is longer) prior to the first dose of BMS-754807 (see the Investigator Brochure)
f) Strong CYP3A4 inhibitors and inducers are prohibited. Subjects must have a wash-out period of at least 5 days or at least 5 half-lives of the drug (whichever is longer) prior to the first dose of BMS-754807 (Please see the Investigator Brochure) A non comprehensive listing of these agents are provided in the IB and can also be accessed at http://medicine.iupui.edu/clinpharm/ddis/table.asp.
g) Chronic use of oral or intravenous corticosteroids (inhalation steroids are allowed). Subjects must have a wash-out period of at least 5 days or at least 5 half-lives of the drug (whichever is longer) prior to the first dose of BMS-754807.

Other Exclusion Criteria
a) Prisoners or subjects who are involuntarily incarcerated
b) Subjects who are compulsorily detained for treatment of either a psychiatric or physical (eg, infectious disease) illness.

Eligibility criteria for this study have been carefully considered to ensure the safety of the study subjects and to ensure that the results of the study can be used. It is imperative that subjects fully meet all eligibility criteria.

Principal Investigator: Gorbaty, Mayer
Phase: II
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Approved Enrollment Number: 4
Current Enrollment: 0
Title: Phase II placebo-controlled trial of lisinopril and Coreg CR® to reduce cardiotoxicity in patients with breast cancer receiving (neo)adjuvant chemotherapy with trastuzumab (Herceptin®) (SCUSF 0806)

Purpose: To compare the effects, good and/or bad, of an ACE inhibitor (lisinopril) or a beta-blocker (Coreg CR® [carvedilol phosphate extended release]) on heart function during treatment with trastuzumab (Herceptin®).

Eligibility: 
- Females 18 years or older diagnosed with HER2 positive breast cancer
- Scheduled to receive neoadjuvant or adjuvant trastuzumab (Herceptin®) therapy (anthracycline-containing regimens are permitted). Patients receiving Herceptin® with their chemotherapy are permitted for eligibility work-up. Taxanes are permitted. Trastuzumab (Herceptin®) therapy may be given with or after primary chemotherapy.
- Left Ventricular Ejection Fraction (LVEF) 50% or more by MUGA scan or echocardiogram
- Normal renal function defined as creatinine 1.2 mg/dL or less
- Sitting systolic blood pressure of more than 90 mm Hg
- Pulse of 60 beats/minute or more
- Not pregnant or breastfeeding
- Patients of childbearing potential, who are sexually active, must have a negative pregnancy test before starting the study, and be willing to use effective contraception during the study. Teratogenicity is documented for both active study agents
- Able to swallow capsules
- Able and willing to give informed consent
- Signed HIPAA compliant research authorization (or equivalent for international sites) to release Personal Health Information to the SunCoast CCOP Research Base.

Exclusion criteria:
- Prior treatment with trastuzumab or anthracyclines prior to this chemotherapy regimen
- Current treatment with angiotensin converting enzyme (ACE) inhibitors, B-Blockers or digoxin
- Known cardiac history: heart failure, myocardial infarction, radiation-induced cardiac dysfunction
- Known allergy to either ACE inhibitors or B-Blockers
- History of bronchial asthma or related bronchospastic conditions
- Hereditary or idiopathic angioedema
- History of severe hypersensitivity reactions to drugs or other causes, i.e. beestings
- This protocol does not exclude patients who are participating on other investigational studies. Refer to the local IRB guidelines.

Principal Investigator: Gorbaty, Mayer

Phase: II

For more information, contact: Hagy, Melissa
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Approved Enrollment Number: 15
Current Enrollment: 3
Title: GOG 0258: A Randomized Phase III Trial of Cisplatin and Tumor Volume Directed Irradiation Followed by Carboplatin and Paclitaxel vs. Carboplatin and Paclitaxel for Optimally Debulked, Advanced Endometrial Carcinoma.

Purpose: To determine if radiation therapy combined with chemotherapy administered for a total of 4 cycles offers a benefit over chemotherapy alone administered over 6 cycles.

Eligibility: Patients 18 years or older with Surgical Stage III or IVA endometrial carcinoma per FIGO 1988 staging criteria, including clear cell and serous papillary and undifferentiated carcinomas.
- Surgical Stage III disease includes those patients with positive adnexa, tumor invading the serosa, positive pelvic and/or para-aortic nodes, or vaginal involvement. Patients with positive pelvic washings as the only extra-uterine disease are eligible only if the histology is clear cell or serous papillary.
- Surgical stage IVA includes patients with bladder or bowel mucosal involvement, but no spread outside the pelvis.
- Surgery must have included a hysterectomy and bilateral salpingo-oophorectomy. Pelvic lymph node sampling and para-aortic lymph node sampling are optional.

Principal Investigator: Abbas, Fouad M.

Phase: III

For more information, contact: Hagy, Melissa

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Approved Enrollment Number: 10

Current Enrollment: 0