

NCCTG N0937: Phase II Trial of Brostallicin and Cisplatin in Patients with Metastatic Triple Negative Breast Cancer

Fast Facts

Brostallicin provided.

CTCAE v4; RECIST 1.1; AJCC Staging Criteria

Patient Eligibility

Inclusion Criteria

1. Women or men ≥ 18 years of age.
2. Disease and stage
 - a. Histologically or cytologically confirmed adenocarcinoma with clinical evidence of metastatic disease.
 - b. Triple negative breast cancer defined as HER2-(according to current ASCO CAP guidelines [Wolff 2007]), ER- (defined as $\leq 1\%$ by IHC) and PgR- (defined as $\leq 1\%$ by IHC).
3. Prior Treatment: 0 to 4 prior chemotherapy regimens in the metastatic setting.
4. Measurable disease according to RECIST criteria (see Section 11.0).
5. Negative pregnancy test done ≤ 7 days prior to registration, for women of childbearing potential only.
6. The following laboratory values obtained ≤ 15 days prior to registration:
 - a. Hemoglobin ≥ 10.0 g/dL
 - b. ANC $\geq 1500/\text{mm}^3$
 - c. Platelet coun $\geq 100,000/\text{mL}$
 - d. Total bilirubin $\leq 1.5 \times \text{ULN}$
 - e. Serum creatinine ≤ 1.5 mg/dL
 - f. SGOT (AST) and SGPT (ALT) $\leq 3 \times \text{ULN}$ or SGOT (AST) and SGPT (ALT) $\leq 5 \times \text{ULN}$ if elevations are due to liver metastases
 - g. Alkaline phosphatase $\leq 2.5 \times \text{ULN}$ or alkaline phosphatase $\leq 5 \times \text{ULN}$ if elevations are due to liver metastases
7. Electrocardiogram (EKG) completed ≤ 15 days prior to registration.
8. ECOG Performance Status (PS) of 0, 1 or 2.
9. Life expectancy >3 months.
10. Has written informed consent been obtained?
11. Willingness to return to NCCTG enrolling institution for treatment and follow-up.
12. Patient willing to provide blood samples for research purposes

Exclusion Criteria

1. HER2 positive (3+ by IHC or FISH amplified) breast cancer by ASCOICAP guidelines (Wolff, 2007).
2. Estrogen receptor (ER) and/or progesterone receptor (PR/PgR) positive breast cancer (defined as $>1\%$ of either receptor by IHC).
3. Any of the following because this study involves an investigational agent whose genotoxic, mutagenic and teratogenic effects on the developing fetus and are unknown
 - a. Pregnant women
 - b. Nursing women
 - c. Men or women of childbearing potential who are unwilling to employ adequate contraception (as determined by the treating physician) while on this study and for 30 days after end of treatment with the study drugs
4. Stage III or IV invasive non-breast malignancy, in ≤ 5 years prior to registration.
5. Pre-existing peripheral neuropathy of Grade ≥ 2 (using the CTEP Active version of the CTCAE).
6. Major surgery ≤ 4 weeks prior to registration.
7. Chemotherapy or immunologic therapy ≤ 3 weeks prior to registration.
8. Radiotherapy ≤ 2 weeks prior to registration, except if to a non-target lesion only.

NOTES: Prior radiation to a target lesion is permitted only if there has been clear progression of the lesion since radiation was completed. If patient receives single dose radiation for palliation or radiation to nontarget lesion, they may immediately proceed to registration without waiting 2 weeks. Acute adverse

events from radiation must have resolved to \leq Grade 1 (according to the CTEP Active Version of the CTCAE).

9. Evidence of active brain metastasis including leptomeningeal involvement.
NOTE: CNS metastasis controlled by prior surgery and/or radiotherapy is allowed. To be considered controlled, there must be at least 2 months of no symptoms or evidence of progression prior to study entry and corticosteroid therapy given to control brain edema must have been discontinued.
10. History of allergy or hypersensitivity to the drugs used in this study (or their excipients) including platinum compounds (cisplatin, carboplatin).
11. Active, unresolved infection.
12. Uncontrolled intercurrent illness including, but not limited to psychiatric illness/social situations or 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 would interfere significantly with the proper assessment of safety of the prescribed regimens or would limit compliance with study requirements or would make it undesirable for patient to participate in the trial.
13. Clinically significant cardiovascular or cerebrovascular disease, including any history of the following \leq 6 months prior to registration:
 - a. Myocardial infarction
 - b. Unstable angina
 - c. New York Heart Association (NYHA) Class II or greater congestive heart failure
 - d. Uncontrolled or clinically significant cardiac arrhythmia (patients with controlled atrial fibrillation are eligible)
14. Currently receiving treatment in a different clinical study in which investigational procedures are performed or investigational therapies are administered.
NOTE: Patient may not enroll in such clinical trials while participating in this study. Exception may be granted for trials related to symptom management (Cancer Control) which do not employ hormonal treatments or treatments that may block the path of the targeted agents used in this trial.
15. Immunocompromised patients (other than that related to the use of corticosteroids) including patients known to be HIV positive with an AIDS defining illness. HIV positive patients with CD4 count within institutional normal range and no history of an AIDS-defining illness are eligible.

Pre-study Parameters

1. History and physical including weight, vital signs, performance status, list of concomitant medications, smoking status, adverse event assessment
2. Labs including CBC with differential and CMP. Pregnancy for women of childbearing potential.
3. EKG
4. The following if clinically indicated: bone scan or PET scan, CT or MRI brain, CT chest, abdomen and pelvis. Scans for tumor measurement must be obtained.
5. Mandatory research blood sample

Treatment

See section 7.0 for complete treatment schedule and required pre-meds. Brostallicin provided.

Cisplatin	50 mg/m ²	IV	Day 1	Every 3 weeks
Brostallicin	10 mg/m ²	IV	Day 2	Every 3 weeks