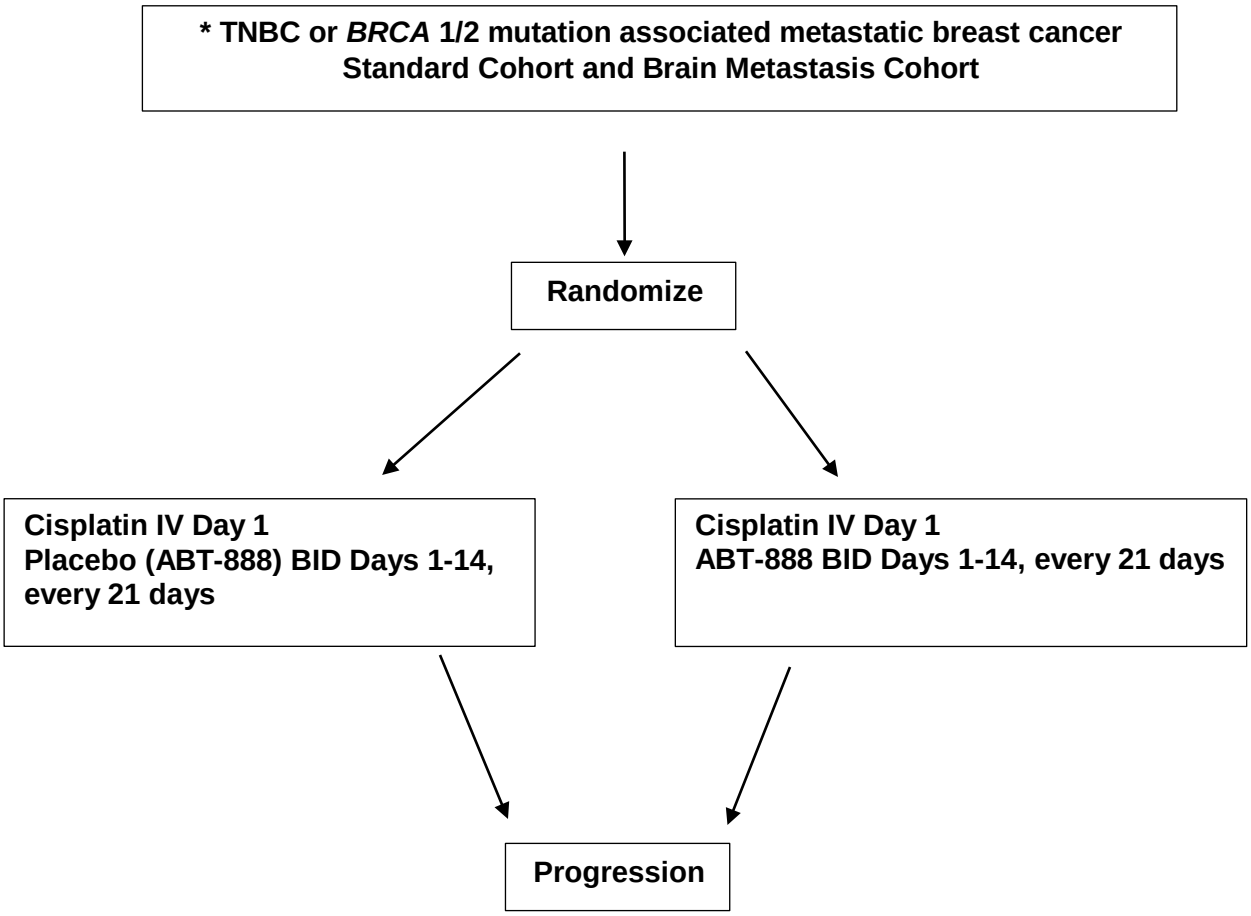
SCHEMA



* **All patients will have germline *BRCA* testing (BROCA-HR) after randomization and then will be assigned to the appropriate groups for analysis based on germline *BRCA* status**
- **BRCA testing results provided to the enrolling physician in 4-8 weeks**
- **Genetic counseling services available for patients if needed (provided by Dr. Swisher, Appendix 18.5)**

Treatment assignment at randomization is not affected by this classification.

5.0 ELIGIBILITY CRITERIA

Each of the criteria in the following section must be met in order for a patient to be considered eligible for registration. Use the spaces provided to confirm a patient's eligibility. For each criterion requiring test results and dates, please record this information on the Onstudy Form and submit via Medidata Rave® (see Section 14.0). Any potential eligibility issues should be addressed to the Data Operations Center in Seattle at 206/652-2267 or breastquestion@crab.org prior to registration.

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday 3 weeks later would be considered Day 21. This allows for efficient patient scheduling without exceeding the guidelines. **If Day 21, 42 or 56 falls on a weekend or holiday, the limit may be extended to the next working day.**

SWOG Patient No. _____

Patient's Initials (L, F, M) _____

5.1 Disease Related Criteria

_____ a. Patients must have metastatic breast cancer and be HER2 non-over expressing per 2013 ASCO-CAP HER testing guidelines (0 or 1+ by IHC; and/or HER2 ratio < 2.0 and HER2 copy number < 4 signals/cell by ISH).

_____ b. Patients must also meet at least one of the following criteria:

1) Triple Negative: Histologically confirmed primary and/or metastatic site that is ER-negative (≤ 1%), PR-negative (≤ 1%), and HER2–negative.

2) *BRCA* mutation: Previously confirmed deleterious *BRCA*1 or *BRCA*2 germline mutation or suspected deleterious BRCA1 or BRCA2 germline mutation if the classification being used is the 5-tier classification. Documentation of germline test results are required.

_____ c. Patients must have measurable or non-measurable disease (see Section 10.1). Patients must have a chest/abdominal/pelvis CT scan (or PET/CT of diagnostic quality, conventional or spiral) and bone scan prior to registration. If the patient is unable to undergo CT with IV contrast due to allergy or renal insufficiency, a non-contrast CT may be performed. All scans needed for assessment of measurable disease must be performed within 28 days prior to registration. Non-measurable disease must be assessed within 42 days prior to registration. All disease must be assessed and documented on the Baseline Tumor Assessment Form.

_____ d. Patients must be women or men ≥ 18 years of age.

_____ e. Patients must have adequate tissue available, must agree to have specimens submitted for germline DNA sequencing and other correlative studies and must submit as per Sections 15.1, 15.2, 15.3 and 15.4.

5.2 Prior/Concurrent Therapy Criteria

_____ a. Patients must have had ≤ 1 prior cytotoxic regimen for metastatic disease.

_____ b. Patients must have completed any prior radiation therapy and hormonal therapy at least 14 days prior to registration.

SWOG Patient No. _____

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5.2 Prior/Concurrent Therapy Criteria (contd.)

_____ c. Patients must not have received prior cisplatin or PARP inhibitors. Prior carboplatin in the adjuvant/neoadjuvant setting is allowed, if completed more than 12 months prior to study entry.

_____ d. Patients must not have received any chemotherapy within 14 days prior to registration.

_____ e. Patients must not have received any immunotherapy, biologic or any investigational drug within 28 days prior to registration. Patients must not have received bevacizumab within 42 days prior to registration.

_____ f. Patients may receive bisphosphonates or denosumab concurrently with study treatment provided it has been started at least 7 days prior to registration.

_____g. Patients must have recovered to ≤ Grade 2 following a significant adverse event or toxicity attributed to previous anti-cancer treatment except neurotoxicity which must be ≤ Grade 1.

5.3 Clinical/Laboratory Criteria

_____ a. Patients must have a performance status of 0-2 by Zubrod criteria (see Section 10.4)

_____ b. Patients must have adequate bone marrow function, as defined by Absolute Neutrophil Count (ANC) of >/= 1,500/mcL, hemoglobin >/= 9 g/dL and a platelet count >/= 100,000/ mcL within 21 days prior to registration.

_____ c. Patients must have adequate hepatic function obtained within 21 days prior to registration and documented by all of the following:

- Bilirubin ≤ 1.5 mg/dL (or ≤ 3.0 mg/dL if due to Gilbert's Syndrome or if liver metastases are present)
- ALT and AST ≤ 2.5 x Institutional Upper Limit of Normal (IULN) (or ≤ 5 x IULN if liver metastases are present)

_____ d. Patients must have adequate renal function with serum creatinine level ≤ IULN within 21 days prior to registration.

_____ e. Patients must have serum chemistries (including potassium and magnesium) done within 21 days prior to registration to obtain baseline values.

_____f. Patients must not have a clinically relevant hearing impairment ≥ Grade 2.

_____ g. Patients must be able to swallow whole capsules.

_____ h. Patients with a history of uncontrolled seizure disorder; including focal or generalized seizure may not have had a seizure within one year prior to registration.

SWOG Patient No. _____

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5.3 Clinical/Laboratory Criteria (contd.)

____i. Patients with known brain metastases must either meet the additional criteria in Section 5.5 and enroll as part of the Brain Metastases Cohort, or else have clinically controlled neurologic symptoms, defined as surgical excision and/or radiation therapy followed by 14 days of stable neurologic function prior to registration. Patients with previously treated progressive brain metastases are not eligible for the Standard Cohort, but may be considered for the Brain Metastases Cohort (see Section 5.5).

_____ j. Patients must not have any incidence of or uncontrolled medical illness (e.g. active cardiac symptoms, active systemic infection, etc.) that would limit the patient's ability to participate in the protocol.

_____ k. Patients must not have baseline peripheral neuropathy that exceeds Grade 1.

_____ l. Patients must have a complete history and physical examination within 28 days prior to registration.

_____ m. Patients of childbearing potential must not be pregnant (negative pregnancy test) or nursing due to the possibility of harm to a fetus or nursing infant from this treatment regimen. Men and women of reproductive potential must have agreed to use an effective contraceptive method for 6 months after completion of study treatment. A woman is considered to be of "reproductive potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation. However, if at any point a previously celibate patient chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures.

_____ n. 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 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 five years.

5.4 Regulatory Criteria

_____ a. Patients 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.

_____ b. As a part of the OPEN registration process (see Section 13.3 for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

SWOG Patient No. _____

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5.5 Brain Metastases Cohort

In addition to all of the previous eligibility criteria, patients with progressive brain metastases who do not satisfy the conditions in Section 5.3h to enroll in the Standard Cohort (neurologic stability for 14 days following surgery and/or radiation therapy) must also meet the following criteria to enroll as part of the Brain Metastases Cohort:

a. Patients with progressive brain metastases must have a baseline brain MRI within 28 days prior to registration. Brain metastases must be progressive and ≥ 10 mm in longest dimension on radiographic imaging AFTER prior intracranial radiation (IR) therapy (i.e., WBRT, SRS, GK or local equivalent). Patients must not have evidence of diffuse leptomeningeal disease on brain MRI or by previously documented CSF cytology. Discrete dural metastases are permitted. There must be no evidence of hemorrhage or impending herniation on baseline brain imaging. Patients with contraindication to gadolinium-enhanced MRI imaging are not eligible.

b. Patients must be on a stable or decreasing dose of steroids for ≥ 7 days prior to registration.

c. If patient has had an open brain biopsy, at least 28 days must have elapsed between biopsy and registration.