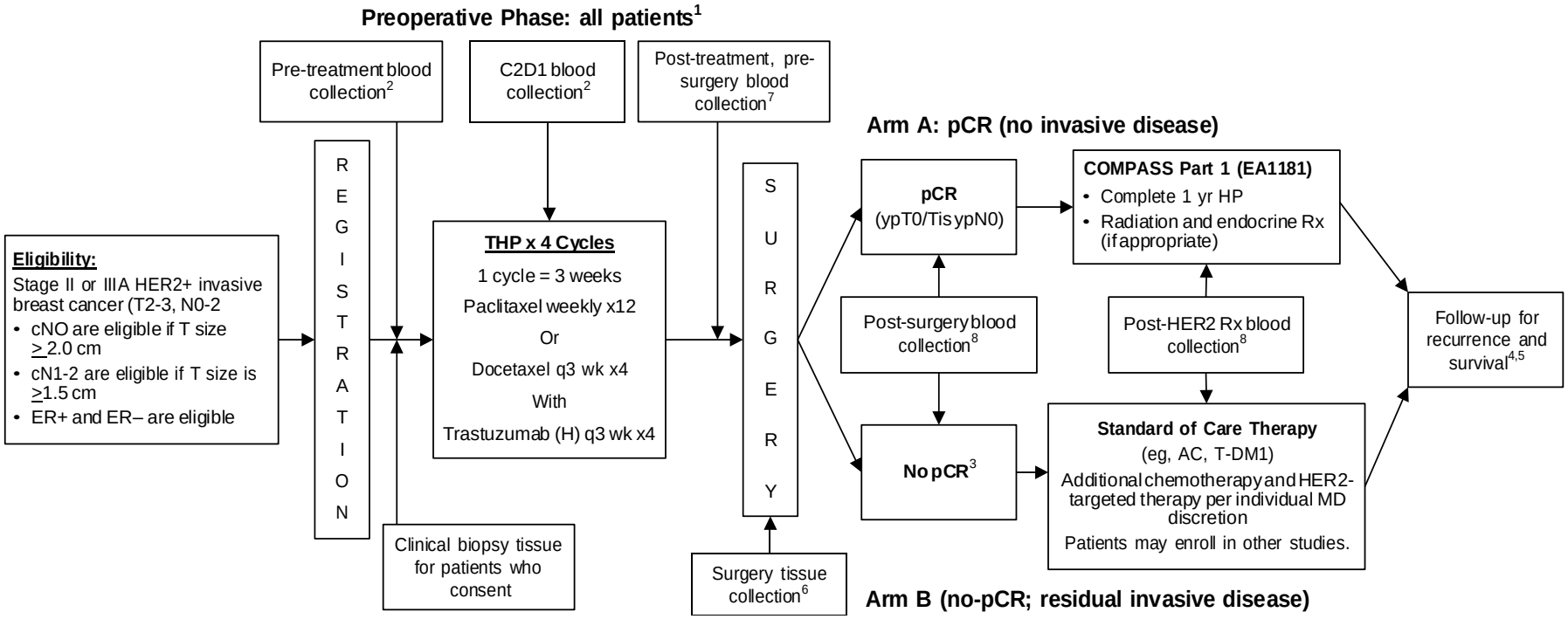
Schema



1. The choice of taxane is up to the treating MD. For patients who develop hypersensitivity to paclitaxel or docetaxel, nab-paclitaxel is permitted.
2. 2 streck tubes for CTCs (mandatory); 2 additional streck tubes for cfDNA for patients who consent.
3. Isolated tumor cells (ITCs) or immunohistochemistry (IHC) evidence of cancer in nodes will be classified as no pCR (Arm B); IHC of nodes is not required. DCIS is allowed.
4. Follow-up: Patients will be followed every 3 months for first 2 years after surgery, then every 6 months if the patient is 2-5 years from surgery, and then every 12 months if the patient is 5-15 years from date of surgery.
5. Primary objective is 3y RFS for patients who achieve pCR. Secondary objectives include 3 yr RFS for those without pCR and (for all patients): EFS, iDFS, DDFS, RFI, OS.
6. Surgery tissue collection for patients who consent.
7. Research blood collection: 2 streck tubes for CTCs.
8. 2 streck tubes for CTCs (mandatory); 2 additional streck tubes for cfDNA in patients with pCR who consent.

3. Selection of Patients

Each of the criteria in the checklist that follows must be met in order for a patient to be considered eligible for this study. Use the checklist to confirm a patient's eligibility. For each patient, this checklist must be photocopied, completed and maintained in the patient's chart.

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 four weeks later would be considered Day 28.

ECOG-ACRIN Patient No. _____

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

Physician Signature and Date _____

NOTE: CTEP Policy does not allow for the issuance of waivers to any protocol specified criteria (http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm). Therefore, all eligibility criteria listed in Section 3 must be met, without exception. The registration of individuals who do not meet all criteria listed in Section 3 can result in the participant being censored from the analysis of the study, and the citation of a major protocol violation during an audit. All questions regarding clarification of eligibility criteria must be directed to the Group's Executive Officer (EA.ExecOfficer@jimmy.harvard.edu) or the Group's Regulatory Officer (EA.RegOfficer@jimmy.harvard.edu).

NOTE: Institutions may use the eligibility checklist as source documentation if it has been reviewed, signed, and dated prior to registration by the treating oncologist.

3.1 Eligibility Criteria

_____ 3.1.1 Patient must be ≥ 18 years of age.

_____ 3.1.2 Patients must have an ECOG performance status of 0 or 1.

_____ 3.1.3 Patient must have histologically confirmed HER2-positive primary invasive breast carcinoma, as defined by the 2018 ASCO/CAP HER2 testing guideline focused update (Wolff et al, 2018) and determined by local testing.

_____ 3.1.4 Patients hormone receptor (ER and PR) status must be known and will be determined by local testing. Patients with either hormone receptor –positive or hormone receptor- negative HER2-positive breast cancer are eligible.

_____ 3.1.5 Patients must have clinical stage II and IIIa (T2-3/N0-2/M0) at diagnosis.

- Patients without nodal involvement (cN0) are eligible if T size ≥ 2.0 cm
- Patients with nodal involvement (cN1-2) are eligible if T size ≥ 1.5 cm

_____ 3.1.6 Patient must be willing and able (i.e., have no contraindication) to receive standard adjuvant therapy, consisting of HER2-directed

therapy, radiation (if indicated) and endocrine therapy (if ER+) if achieving pCR at surgery.

_____ 3.1.7 Patient with two separate invasive breast cancers (ipsilateral or bilateral) are eligible if both cancers are HER2-positive (as defined in 3.1.3) and at least one meets protocol eligibility (i.e., ≥ 1.5 cm if cN1-2; ≥ 2 cm if cN0) (neither tumor can be T4 or N3).

_____ 3.1.8 Patients with multifocal or multicentric disease are eligible as long as all tumor foci that were tested for HER2 status at the local institution are HER2-positive, and at least one tumor focus meets eligibility criteria.

_____ 3.1.9 Patients must not have impaired decision-making capacity.

_____ 3.1.10 Patient must not have a history of any prior (ipsilateral or contralateral) invasive breast cancer.

One exception: a patient with a history of T1N0 triple negative breast cancer diagnosed more than 10 years earlier, who remains disease free is eligible.

_____ 3.1.11 Patient must not have prior ipsilateral DCIS. Patients with prior LCIS, atypical hyperplasia, other high risk benign lesions or contralateral DCIS (without evidence of microinvasion) are eligible.

NOTE: Patients currently receiving endocrine therapy for prior contralateral DCIS are eligible.

_____ 3.1.12 Patient must not have Stage IV (metastatic) breast cancer.

Staging Studies (CT Chest/abdomen/pelvis and a bone scan or PET-CT scan) are required for Stage III disease or those with abnormal baseline LFTs, symptoms (e.g. new bone pain) or abnormal physical exam findings (NCCN guidelines V1.2019).

_____ 3.1.13 Patient must not have T4 and/or N3 disease, including inflammatory breast cancer.

_____ 3.1.14 Patient must not have any prior treatment for the current breast cancer, including surgery, chemotherapy, hormonal therapy, radiation or experimental therapy.

_____ 3.1.15 Patients with a history of other non-breast malignancies are eligible if they have been disease-free for at least 5 years, and are deemed by the investigator to be at low risk for recurrence of that malignancy.

Patients with the following cancers are eligible if diagnosed and treated within the past 5 years: cervical cancer in situ, basal cell or squamous cell carcinoma of the skin, and localized papillary or follicular thyroid cancer who have completed recommended treatment including surgery. Patients with any other cancers within the last 5 years are ineligible.

_____ 3.1.16 Patents must have a left ventricular ejection fraction (LVEF) within normal institutional parameters (or > 50%).

_____3.1.17 Patients must not have > grade 1 peripheral neuropathy of any etiology.

_____ 3.1.18 Patients must have a bilateral mammogram and diagnostic breast ultrasound (with or without breast MRI) performed at screening (within 42 days of registration)

_____3.1.19 Baseline imaging of the ipsilateral axilla by ultrasound is mandatory. For subjects with axillary lymph node(s) suspicious on clinical exam or imaging, patient must be willing to have a needle aspiration or core biopsy to determine the presence of metastatic disease in the lymph nodes. A clip must be placed in the involved axillary lymph node.

_____3.1.20 Patient must not have a concurrent serious medical condition that would preclude completion of study therapy. For example, uncontrolled hypertension (systolic >180 mm Hg and/or diastolic >100 mm Hg) or clinically significant (i.e. active) cardiovascular disease: cerebrovascular accident/stroke or myocardial infarction within 6 months prior to registration, unstable angina, congestive heart failure (CHF) or serious cardiac arrhythmia requiring medication and other concurrent serious diseases that may interfere with planned treatment.

_____3.1.21 Women must not be pregnant or breast-feeding due to the potential harm to an unborn fetus and possible risk for adverse events in nursing infants with the treatment regimens being used. Patients must also not expect to conceive from the time of registration, while on study treatment, and until at least 7 months after the last dose of study treatment.

All females of childbearing potential must have a blood test or urine study within 14 days prior to registration to rule out pregnancy.

A female of childbearing potential is any woman, regardless of sexual orientation or whether they have undergone tubal ligation, who meets the following criteria: 1) has achieved menarche at some point, 2) has not undergone a hysterectomy or bilateral oophorectomy; or 3) has not been naturally postmenopausal for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months).

Female of childbearing potential?_____(Yes or No)

Date of blood test or urine study: _____

_____3.1.22 Women of childbearing potential and sexually active males must use accepted and effective method(s) of contraception or to abstain from sexual intercourse for the duration of their participation in the study and for 7 months after the last dose of study treatment.

_____ 3.1.23 Patient must be willing and able to sign informed consent.

_____3.1.24 Patients must have adequate organ and marrow function as defined below (these must be obtained ≤ 28 days prior to protocol registration).

_____ Leukocytes ≥ 3,000/mcL

Leukocytes:_____Date of Test:_____

_____ Absolute neutrophil count ≥ 1,500/mcL

_____

_____

ANC:_____Date of Test:_____

Platelets ≥ 100,000/mcL

Platelet:_____Date of Test:_____

Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN)

Bilirubin:_____Institutional ULN:_____

Date of Test:_____

AST(SGOT)/ALT(SGPT) ≤ 2.5 x institutional ULN

ALT:_____Institutional ULN:_____

Date of Test:_____

AST:_____Institutional ULN:_____

Date of Test:_____

_____Creatinine ≤ 1.5 x institutional ULN

Serum creatinine_____Date of Test:_____

_____3.1.25 Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial.

_____3.1.26 For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.

_____3.1.27 Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load.

_____ _____

Physician Signature Date

OPTIONAL: This signature line is provided for use by institutions wishing to use the eligibility checklist as source documentation.