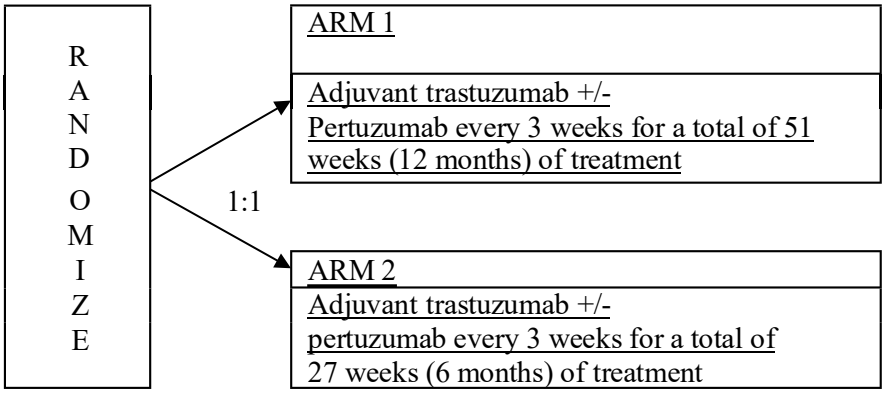
SHORTSTOP-HER2: SHORTENED DURATION OF ADJUVANT THERAPY IN PATIENTS WITH EARLY-STAGE HER2+ BREAST CANCER WHO ACHIEVE PCR AFTER NEOADJUVANT CHEMOTHERAPY WITH HER2 BLOCKADE

Eligibility Criteria

-History of clinical tumor category T1c-T3 and clinical nodal category N0-N1 (except cT3N1 tumors, which are NOT eligible) per AJCC 8th edition
-HER2+ by ASCO/CAP guidelines (See Section 3.2.1)
- Pathologic complete response following neoadjuvant therapy
-Age ≥ 18 years
-ECOG Performance Status 0-2
-Prior treatment per Section 3.2.4
-Surgery requirements per Section 3.2.5
-Not pregnant and not nursing
-Adequate hepatic, renal and bone marrow function for therapy
-No comorbid conditions per Section 3.2.8.

Schema



The total duration of treatment includes the treatment received prior to A012303 registration. Treatment is to continue for the specified time per protocol, or until unacceptable adverse event. Patients will be followed for 10 years or until death, whichever comes first.

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.

3.0 PATIENT SELECTION

For questions regarding eligibility criteria, see the Study Resources page. Please note that the Study Chair cannot grant waivers to eligibility requirements.

3.1 On-study Guidelines

This clinical trial can fulfill its objectives only if patients appropriate for this trial are enrolled. All relevant medical and other considerations should be taken into account when deciding whether this protocol is appropriate for a particular patient. Physicians should consider the risks and benefits of any therapy, and therefore only enroll patients for whom this treatment is appropriate.

Physicians should consider whether any of the following may render the patient inappropriate for this protocol:

Women and men of reproductive potential should agree to use an appropriate method of birth control throughout their participation in this study and for 7 months following the last dose of study treatment due to the teratogenic potential of the therapy utilized in this trial. Appropriate methods of birth control include abstinence, oral contraceptives, implantable hormonal contraceptives or double barrier method (diaphragm plus condom). Breastfeeding should also be discontinued during study treatment and for 7 months following the last dose of study treatment.

3.2 Registration Eligibility Criteria

Use the spaces provided to confirm a patient's eligibility by indicating Yes or No as appropriate. It is not required to complete or submit the following page(s). Please note that an optional signature line has been provided for use by institutions wishing to use the eligibility checklist as source documentation.

When calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test were done on a Monday, the Monday one week later would be considered Day 7.

A female of childbearing potential is a sexually mature female who: 1) has not undergone a hysterectomy or bilateral oophorectomy; or 2) has not been naturally postmenopausal for at least 12 consecutive months (i.e., has had menses at any time in the preceding 12 consecutive months).

___3.2.1 Documentation of Disease

__3.2.1.1 Patients (females and males) with clinical stage T1c-T3 (or Tx) and nodal stage N0-N1 (**except T3N1 tumors, which are *not* eligible**)

__3.2.1.2 Patients must have no residual invasive disease in the breast or lymph nodes after the completion of neoadjuvant therapy. Residual DCIS is allowed. Patients with residual isolated tumor cells at surgery are considered node-positive and are *not* eligible.

__3.2.1.3 HER2+ by ASCO/CAP guidelines. Central pathology review is *not* required. In cases where there were multiple tumor sites in breast/nodes that had HER2 testing at diagnosis, at least one site must have been HER2+ AND the treating investigator must feel it is in the patient's best interest to be treated as having HER2+ breast cancer.

__3.2.1.4 Known hormone receptor status as defined by ASCO/CAP guidelines. ER and PR of any values are allowed. Hormone receptor positive status can be

determined by either known positive ER or known positive PR status; hormone receptor negative status must be determined by both known negative ER and known negative PR.

3.2.1.5 If invasive disease was present in both breasts, participation in the study is permitted as long as the eligibility criteria are met for both tumors/breasts (including the requirement that at least one biopsied site on each side must have been HER2+).

3.2.2 Age ≥ 18 years

3.2.3 ECOG Performance Status 0-2

3.2.4 Prior Treatment

3.2.4.1 Patients must have received neoadjuvant chemotherapy in combination with trastuzumab with or without pertuzumab for a minimum of 12 weeks. All chemotherapy must have been completed preoperatively.

Patient must complete a minimum of 12 weeks of coverage with trastuzumab and a maximum of 24 weeks in the combined neoadjuvant and adjuvant setting prior to trial registration. Trastuzumab may have been administered either weekly or q3weeks. (For purposes of this eligibility criterion, a single dose of q3week trastuzumab would provide 3 weeks of coverage; a single dose of q1week trastuzumab would provide 1 week of coverage. If a q3week dose of trastuzumab were administered and then the subsequent dose was delayed for any period of time, that would still count as 3 weeks of coverage.)

Administration of endocrine therapy for treatment of this breast cancer is allowed prior to trial registration. If a patient received prior breast cancer endocrine therapy (eg tamoxifen or aromatase inhibitor) for DCIS or preventive indication, and endocrine therapy is indicated for treatment of their current breast cancer, then prior endocrine therapy must have been stopped >12 months prior to registration on this protocol.

No use of investigational anti-cancer agents at time of registration.

3.2.4.2 Patient must register within 14 weeks of final surgery.

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___3.2.5 Surgery Requirements

_3.2.5.1 Adequate excision: surgical removal of all clinically evident disease in the breast and lymph nodes as follows:

- Breast surgery: total mastectomy with grossly negative margins (in the opinion of the surgeon there is no disease grossly at the margins) or breast-conserving surgery with histologically negative margins (no ink on tumor, including DCIS) unless those margins are anterior at the skin or posterior at the chest wall and no additional margin re-excision can be performed.
- Lymph node surgery: Lymph node surgery must have been performed and can include sentinel lymph node biopsy, targeted axillary dissection, or axillary dissection, at the discretion of the breast surgeon.

___3.2.5.2 Pre-Registration Radiation

Adequate radiation: Patients who completed breast-conserving surgery (i.e. lumpectomy) must have received or plan to receive adjuvant radiation. If breast-conserving surgery was performed but patient will not be receiving breast radiation, the patient is not eligible. Patients for whom radiotherapy would be recommended for breast cancer treatment but for whom it is contraindicated because of medical reasons (e.g., connective tissue disorder or prior ipsilateral breast radiation) are not eligible.

- Adjuvant radiation can be given on study, and in this case is encouraged to be given concurrently with adjuvant HER2-directed therapy, per investigator discretion.
- Targeting of the regional nodal basins will be at treating Investigator discretion.

_3.2.6 Not pregnant and not nursing, because this study involves agents with known teratogenic potential. Therefore, for women of childbearing potential only, a negative serum or urine pregnancy test should be performed prior to receiving HER2-directed therapy according to local standard practice.

_3.2.7 Adequate hepatic, renal and bone marrow function to receive adjuvant HER2-directed therapy in the opinion of the treating investigator. There are no specific required laboratory values for eligibility**.**

___3.2.8 Comorbid conditions

___3.2.8.1 No stage IV (metastatic) breast cancer.

__3.2.8.2 Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

___3.2.8.3 No history of any prior (ipsi- or contralateral) invasive breast cancer. Prior DCIS is allowed.

___3.2.8.4 No evidence of recurrent disease following preoperative therapy and surgery.

___3.2.8.5 Patients living with HIV who are healthy and deemed by their medical team to have a low risk of AIDS-related illnesses are included in this trial. Patients with Hepatitis B or Hepatitis C virus who are healthy and deemed by their medical team to meet all other enrollment criteria are included in this trial.

__3.2.8.6 Patients with inadequate cardiac function on most recent assessment of left ventricular ejection fraction (LVEF) are not eligible for this trial. Inadequate cardiac function is defined as LVEF < 50% on echocardiogram (echo) or multiple-gated acquisition (MUGA).

__3.2.8.7 No history of grade 3 or 4 toxicity related to trastuzumab. If pertuzumab is planned to be given on trial, patient must also have no history of grade 3-4 toxicity related to pertuzumab.

___3.2.8.8 No contraindication to receipt of further HER2-directed therapy.

___3.2.8.9 No patients with severe, uncontrolled systemic disease that may interfere with planned trial therapy.

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