NCI National Clinical Trials Network

EA1181/CompassHER2 pCR

For Patients with HER2 positive Breast Cancer

EA1181 Available Through ECOG-ACRIN Cancer Research Group

Preoperative THP & Postoperative HP in Patients who Achieve a Pathologic Complete Response

Part 1 Component of: *The CompassHER2 Trials (COMprehensive use of Pathologic response ASSessment to optimize therapy in HER2 positive breast cancer)*

Patient Population

See Section 3.0 for Complete Eligibility Details

- Age ≥ 18 years, ECOG PS 0-1, and adequate lab values
- Must have histologically confirmed HER2+ primary invasive breast carcinoma determined by local testing
  - ◊ Tumor must have either HER2 IHC result of 3+ or HER2/CEP17 ratio >2 with >4.0 HER2 signals per cell by ISH (see protocol for details)
- ER and PR status must be known/determined by local testing; patients with hormone receptor postitive/ negative HER2+ breast cancer are eligible
- Must have AJCC 8th ed. stage II/IIIa per anatomic staging table at diagnosis (see protocol for details)
- Must have no contraindication to standard adjuvant therapy, consisting of HER2 directed therapy, radiation (if indicated) and endocrine therapy (if ER+) if achieving pCR at surgery
- Patients with bilateral invasive breast cancers, or with multiple ipsilateral invasive tumors are eligible per protocol
- Must not have prior invasive breast cancer, or ipsilateral DCIS (see protocol for details/exceptions)
- No prior treatment for the current breast cancer
- LVEF within normal institutional parameters (or ≥ 50%)
- No > grade 1 peripheral neuropathy (any etiology)
- Must have a bilateral mammogram and a diagnostic breast ultrasound [on the side of the cancer(s)] (with or without breast MRI) at screening; an axillary ultrasound on the side of the cancer(s) is also required
  - ◊ Comprehensive breast and axillary imaging must be performed within 60 days of registration (mammogram/breast ultrasound/axillary ultrasound OR breast MRI)
- Must not have a concurrent serious medical condition that would preclude completion of study therapy (see protocol for examples)
- HIV, HBV, and HCV patients are permitted per protocol

Treatment Plan

See Section 5.0 for Complete Treatment Details

1 cycle= 21 days; treatment to be administered +/- 3 days

Pre-Operative/Neoadjuvant THP:

- Choice of taxane therapy per the treating oncologist:
  - ◊ Option 1: Paclitaxel, Trastuzumab (or FDA approved biosimilar), Pertuzumab, x 4 cycles
  - ◊ Option 2: Docetaxel, Trastuzumab (or FDA approved biosimilar), Pertuzumab, x 4 cycles. Prophylactic growth factor support is required
  - ◊ Option 3: Nab-paclitaxel, Trastuzumab (or FDA approved biosimilar), Pertuzumab, x 4 cycles
- If surgery occurs later than 21 days after the 4th cycle of HP/THP, a 5th/6th cycle of HP (without taxane) must be administered before surgery. Patients who progressed during THP must get additional pre-surgical therapy (per the treating oncologist; followed per Arm B)
- Lumpectomy/mastectomy must be performed no later than 126 days from the first dose of neoadjuvant taxane therapy; axillary surgery per protocol

Post-Operative/Adjuvant Therapy:

- Arm A: pCR (no invasive disease); Trastuzumab/ biosimilar, Pertuzumab for 13 cycles, radiation therapy and endocrine therapy if appropriate (see protocol)
- Arm B: SOC for patients who do NOT achieve pCR

Notes:

- *Doses are based on actual body weight at baseline; one 3 week dose of docetaxel = 3 weekly doses of paclitaxel*
- *Breast imaging is required prior to surgery; a clip must be placed in the breast primary tumor (see protocol)*
- *See protocol for pre-treament tumor evaluation (imaging/ staging/surgical assessment/axillary assessment pre-therapy); and pre-surgery tumor evaluation (imaging/ physical exam evidence of residual disease)*
- *Follow institutional guidelines for infusion order, and preparation/administration/pre-medications for paclitaxel/ nab-paclitaxel*

Study Chair:
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Study Co-Chairs:
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Patient Enrollment

All Sites: Oncology Patient Enrollment Network (OPEN) https://open.ctsu.org

Protocol Information

ECOG-ACRIN Operations-Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

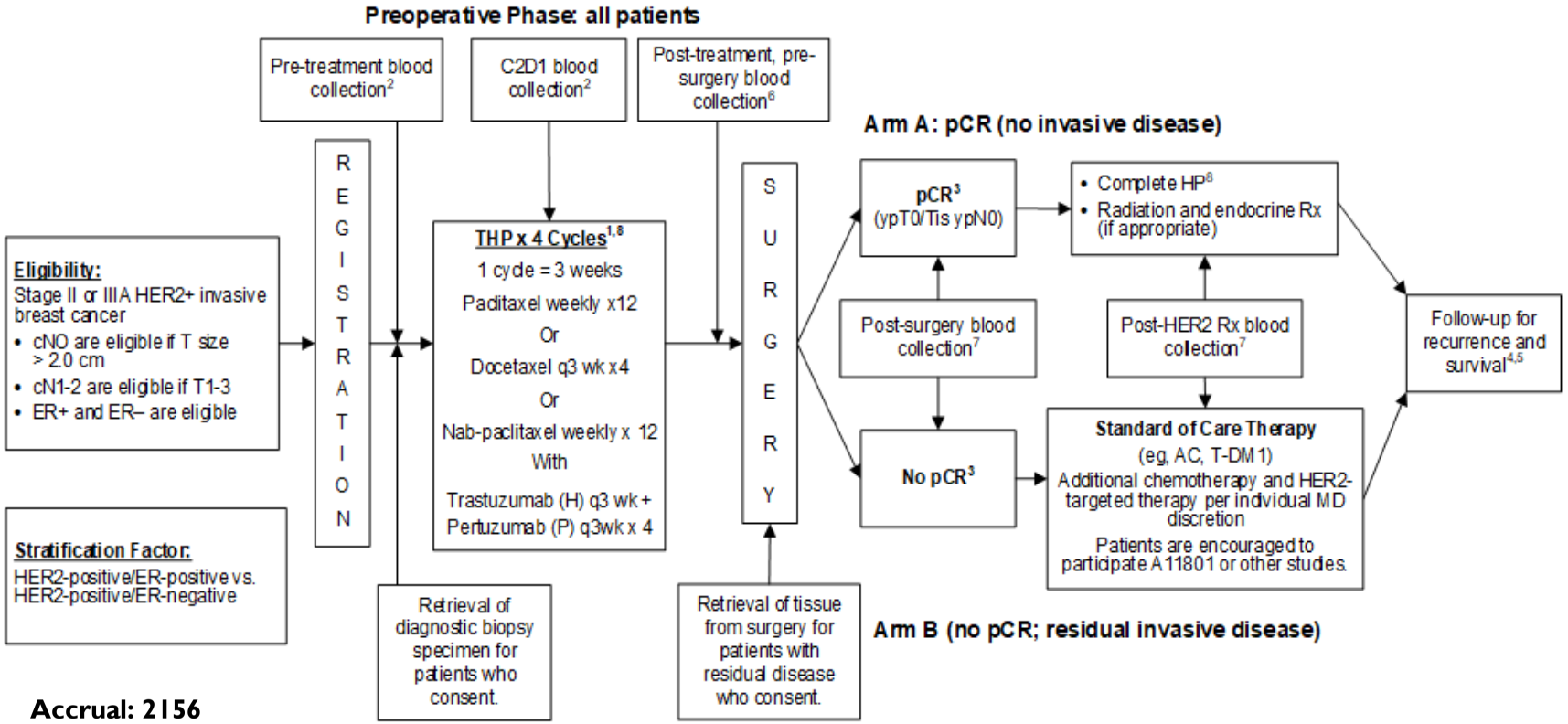
Please Enroll Your Eligible Patients!

Version 02/28/22 (Add. #7)

ECOG-ACRIN cancer research group

EA1181

Schema (CompassHER2 pCR; EA1181; Compass Part 1)



1. The choice of taxane is up to the treating MD. For patients who develop hypersensitivity to paclitaxel or docetaxel, nab-paclitaxel is recommended.
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 in Arm A.
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. Research blood collection: 2 streck tubes for CTCs.
7. 2 streck tubes for CTCs (mandatory); 2 additional streck tubes for cfDNA in patients with pCR who consent.
8. 17 cycles **total** of HP will be administered to patients in Arm A including both pre- and post-surgery cycles. HP should be continued every 3 weeks until surgery, even when taxane therapy has been completed.
9. Trastuzumab-hyaluronidase SC may be substituted for trastuzumab; or pertuzumab-trastuzumab-hyaluronidase SC may be substituted for both trastuzumab and pertuzumab, following the dosing instructions in the US Package Inserts for Herceptin Hylecta® or Phesgo®.