A Randomized Phase III Post-operative Trial of Platinum Based Chemotherapy vs. Capecitabine in Patients With Residual Triple-Negative Breast Cancer Following Neoadjuvant Chemotherapy

Overall Study Goal
To determine whether patients with clinical stage II-III triple-negative breast cancer (TNBC) with ≥ 1 cm of residual disease and basal-like subtype in their surgical specimen after neoadjuvant chemotherapy who are treated with adjuvant platinum-based chemotherapy will have a longer invasive disease-free survival (IDFS) compared with capecitabine, the current standard of care, based on Create-X trial results.

Study Schema

Accrual goal = 750 patients.
Cycle = 3 weeks.
Doses based on actual body weight.
Arm A closed to new accrual; new patients are randomized to arm B or C.

*TNBC: ER/PR < 10% positive staining with weak intensity score, or < 1% positive staining with weak or intermediate intensity score; HER2 negative per ASCO guidelines.
†Taxane ± anthracycline based; platinum agents or capecitabine not allowed.
‡Tumor tissue from residual disease on definitive surgical specimen must be submitted within 21 weeks post surgery for PAM50 analysis for stratification. Patients cannot be randomized to treatment until confirmation of PAM50 analysis from Molecular Diagnostics Laboratory performing the assessments.
§Radiotherapy may be given before protocol treatment but must be completed prior to randomization or deferred until after treatment completion.
||Females of child-bearing potential must have a blood test or urine study within 2 weeks prior to treatment initiation to rule out pregnancy.
¶Choice of platinum agent will be per treating physician discretion.
#Primary end point: IDFS in patients with basal-like TNBC.
**Secondary end points: OS, RFS, safety, rate of basal-like gene expression, IDFS in patients with non-basal-like TNBC, HRQL, rate of neurotoxicity, and rate of capecitabine adherence.
AUC = area under the curve; ER = estrogen receptor; HRQL = health-related quality of life; IDFS = invasive disease-free survival; NAC = neoadjuvant chemotherapy; OS = overall survival; PR = progesterone receptor; PRO = patient-reported outcomes; RFS = relapse-free survival; TNBC = triple-negative breast cancer.

Objectives

Primary Objective
- Compare IDFS in TNBC patients with residual basal-like disease after neoadjuvant chemotherapy who are randomized to post-preoperative platinum-based chemotherapy with those randomized to capecitabine.

Secondary Objectives
- Evaluate overall survival and recurrence-free survival.
- Characterize side effects and tolerability of each platinum agent (cisplatin and carboplatin) and capecitabine.
- Identify rate of basal-like gene expression using PAM50 analysis by digital mRNA quantitation among drug-resistant residual TNBC after neoadjuvant chemotherapy.
- Compare IDFS in TNBC patients with residual non-basal-like disease after neoadjuvant chemotherapy who are randomized to post-preoperative platinum-based chemotherapy with those who are randomized to capecitabine (exploratory analysis).
- Assess the difference in health-related quality of life between platinum-based and capecitabine chemotherapy.
- Describe the rate of neurotoxicity in the platinum arm, rate of capecitabine adherence, and rates of amenorrhea in both arms (exploratory).

Correlative Biomarker Objective
- Evaluate the association of genomic alterations identified via profiling of the surgical tumor specimen with relapse-free survival.

Exploratory Tobacco Use Objectives
Refer to Protocol Section 2.4 for list of objectives.
How Your Site Can Participate

• Before recruitment, investigators must be registered members of an NCTN network
• All individuals contributing to NCI-sponsored trials must register and renew annually
• Registrants must obtain a Cancer Therapy Evaluation Program (CTEP) Identity and Access Management (IAM) account (https://ctepcore.nci.nih.gov/iam)
• Investigator (IVR), Non-physician Investigator (NPIVR), or Associate Plus (AP) must complete annual registration using CTEP’s Web-based Registration and Credential Repository (RCR) (https://ctepcore.nci.nih.gov/rcr)
• Required documentation for IVR, NPIVR, and AP includes FDA Form 1572 (IVR and NPIVR only), Financial Disclosure Form, NCI Biosketch, HSP/GCP training, Agent Shipment Form (IVR only), and CV (optional)
• IVRs and NPIVRs must list clinical practice sites and IRBs covering their practice sites on FDA Form 1572 in RCR to allow the following: added to site roster; assigned treating, credit, consenting, or drug shipment (IVR only) tasks in OPEN; acting as site-protocol Principal Investigator (PI) on IRB approval; assigned Clinical Investigator (CI) role on Delegation of Tasks Log (DTL)
• For questions, please contact RCR Help Desk via e-mail: RCRHelpDesk@nih.gov
• Sites participating on the NCI Central Institutional Review Board (CIRB) initiative that are approved by the CIRB for this study need not submit IRB approval documentation to Cancer Trials Support Unit (CTSU). For sites using CIRB, IRB data automatically load to RSS. Signatory Institutions must submit a Study Specific Worksheet for Local Context (SSW) to CIRB via IRB Manager to indicate intent. CIRB’s approval of SSW is communicated to CTSU Regulatory Office. For SSW approval processing, Signatory Institution must inform CTSU which CIRB-approved institutions aligned with the Signatory Institution are participating

• Requirements for EA1131 site registration:
  – IRB approval
  – For sites not participating via the NCI CIRB: local IRB documentation, an IRB-signed CTSU IRB Certification Form, Protocol of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption Form, or combination is accepted

• Submit all required regulatory documents to the CTSU Regulatory Office via the Regulatory Submission Portal www.ctsu.org (members’ area) → Regulatory Tab → Regulatory Submission
  – When applicable, mail original documents to:
    CTSU Regulatory Office
    1818 Market Street, Suite 3000
    Philadelphia, PA 19103
  – Institutions with patients waiting and unable to use portal, immediately contact CTSU Regulatory Office at (866) 651-2878

• Required regulatory documentation:
  – Copy of IRB Informed Consent Document
  – CTSU IRB Certification form or Signed HHS OMB No. 0990-0263 (replaced Form 310) or IRB Approval Letter

Note: Submission must include all sites approved for the protocol under an assurance number; OHRP assurance number of reviewing IRB; full protocol title and number; version date; type of review (full board vs expedited); date of review; signature of IRB official
• Check registration status at https://www.ctsu.org
• Once documentation has been submitted and approved:
  – Treatment should start within 3 weeks or 15 working days after randomization
  – Patient enrollment is via OPEN, accessed at https://open.ctsu.org. Data collection is through Medidata Rave and ECOG-ACRIN Systems for Easy Entry of Patient Reported Outcomes (EASEE-PRO) System. Address OPEN and Medidata Rave questions to the CTSU Help Desk at 1-888-823-5923 or ctsucontact@westat.com
  – Pathologic materials must be submitted no later than week 21 post-surgery for PAM50 analysis per protocol (Section 10.2). The Molecular Diagnostics Laboratory at MD Anderson Cancer Center notifies ECOG-ACRIN Operations Office of PAM50 analysis results within 3 weeks of receiving tumor tissue specimen. Results will not be reported to the submitting institution. Submission of inadequate specimen leads to a request for additional material and delays turnaround time for reporting results

Contact Information

ECOG-ACRIN Study Chair
Ingrid A. Mayer, MD, MSCI
Vanderbilt University Medical Center/
Vanderbilt-Ingram Cancer Center
2220 Pierce Avenue, 777 PRB
Nashville, TN 37232
Phone: (615) 936-2033
E-mail: Ingrid.mayer@vumc.org

Study Co-Chair
Carlos L. Arteaga, MD
University of Texas Southwestern
Harold C. Simmons Cancer Center
3323 Harry Hines Blvd
Dallas, TX 75390
Phone: (214) 648-1677
E-mail: carlos.arteaga@utswsouthwestern.edu

Study Chair Liaison
Jannine Hewitt, RN
Vanderbilt University Medical Center/
Vanderbilt-Ingram Cancer Center
719 Thompson Lane, Suite 25000
Nashville, TN 37212
Phone: (615) 875-9639
E-mail: jannine.hewitt@vumc.org

For Further Study Information

• For more information about the EA1131 study, please visit the following:
  – Cancer.gov; search EA1131
  – Clinicaltrials.gov; search NCT02445391
• For more information about ECOG-ACRIN, visit ecog-acrin.org