NEW FEATURED TRIAL AT THE SIDNEY KIMMEL CANCER CENTER AT JEFFERSON UNIVERSITY:

Title - MM-302 Plus Trastuzumab vs. Chemotherapy of Physician's Choice Plus Trastuzumab in HER2-Positive Locally Advanced/Metastatic Breast Cancer Patients (HERMIONE)

Sponsor: Merrimack Pharmaceuticals

PI: Massimo Cristofanilli, MD

This study is an open label, randomized, multicenter trial of MM-302 plus trastuzumab. The trial is designed to demonstrate whether MM-302 plus trastuzumab is more effective than the chemotherapy of physician's choice (CPC) plus trastuzumab in locally advanced/metastatic HER2-positive breast cancer patients who have received prior treatment with trastuzumab in any setting and who have either progressed or are intolerant to each of pertuzumab and ado-trastuzumab emtansine in the metastatic or locally advanced setting. Patients must not have been previously treated with an anthracycline in any setting.

Inclusion Criteria:
- Patients must have histologically or cytologically confirmed invasive cancer of the breast
- Patients must have documented locally advanced/metastatic disease, defined by the investigator, which is not amenable to resection with curative intent.
- Patients must have HER2-positive breast cancer as defined by ASCO/CAP 2013 guidelines that is confirmed by a Sponsor-designated central laboratory
- Patients must have progressed on, or be intolerant to pertuzumab in the LABC/MBC setting
- Patients must have progressed on, or be intolerant to ado-trastuzumab emtansine in the LABC/MBC setting
- Patients must have been previously treated with trastuzumab in any setting (which may have been previously administered with or without pertuzumab)
- ECOG Performance Status of 0 or 1

Exclusion Criteria:
- Patients who have previously been treated with doxorubicin, liposomal doxorubicin, epirubicin, mitoxantrone, or any other anthracycline derivative
- Subjects with central nervous system (CNS) metastases, unless they have been treated and are stable without symptoms for 4 weeks after completion of treatment and must be off steroids for at least 4 weeks prior to enrollment

Coordinator Contact: Melisa Mordenti, MPH, Melisa.Mordenti@jefferson.edu, Pager 877-656-1227
NRG-LU001: Randomized Phase II Trial of Concurrent Chemoradiotherapy +/- Metformin HCL in Locally Advanced NSCLC
     PI: Bo Lu, MD

SWOG-1406: Randomized Phase II Study of Irinotecan and Cetuximab with or without Vemurafenib in BRAF Mutant Metastatic Colorectal Cancer
     PI: Christina Brus, MD

EA2212: A Randomized, Double-Blinded, Placebo-Controlled Phase II Study of Adjuvant Everolimus Following the Resection of Metastatic Pancreatic Neuroendocrine Tumors to the Liver

EA8141: A Prospective Phase II Trial of Neoadjuvant Systemic Chemotherapy Followed by Extirpative Surgery for Patients with High Grade Upper Tract Urothelial Carcinoma

EAY131: Molecular Analysis for Therapy Choice (MATCH)

EA1131: A Randomized Phase III Post-Operative Trial of Platinum Based Chemotherapy Vs. Observation in Patients with Residual Triple-Negative Basal-Like Breast Cancer Following Neoadjuvant Chemotherapy

BN001: Randomized Phase II Trial of Hypofractionated Dose-Escalated Photon IMRT or Proton Beam Therapy Versus Conventional Photon Irradiation with Concomitant and Adjuvant Temozolomide in Patients with Newly Diagnosed Glioblastoma

BR002: A Phase IIR/III Trial of Standard of Care Therapy with or Without Stereotactic Body Radiotherapy (SBRT) and/or Surgical Ablation for Newly Oligometastatic Breast Cancer

In an effort to keep the research community informed of new and revised Office of Human Research (OHR) policies and forms, a summary of recent changes is available on the IRB website http://www.jefferson.edu/university/human_research/irb.html. Please remember to always access the most current policies and forms on the Division of Human Subjects Protection page of the OHR website.
**Regulatory Update:**
5/6/15  MAVERICC-Amendment Ltr revisions to consent form only
5/15/15  RTOG 0839-Amendment Ltr revisions to consent form only
5/18/15  ECOG 2108-Amendment Ltr-Addendum #6 revisions to protocol & consent
6/2/15   Astra Zeneca-AZD6344-Amendment Ltr revisions to consent only
6/2/15   ECOG 7208-Amendment Ltr closed to accrual per CCRCC
6/2/15   SWOG 0033 CTEP withdrawal of DCTD sponsored IND #6135 for ST1571 informational
6/9/15   NSABP B50-I Amendment change PI-revisions to consent form

**CTSU cont.**
website has been enhanced to display a list of the recently posted CIRB documents under a new tab called CIRB Updates. The CIRB Updates tab is similar to the CTSU’s Protocol Updates tab and lists newly posted or updated postings of CIRB documents. The document names are clickable links. CIRB document access is limited to individuals on the CIRB roster or the roster of the lead or participating protocol organization.

**NRG UPDATE:**
Semi-annual meeting Online registration deadline is June 26th! Register and access meeting information on the NRG Oncology website.

**NRG-BR001:** Osseous (bone) metastatic site was temporarily closed to accrual on June 9; however, the other six metastatic locations including spinal/paraspinal remain open.

**NSABP B52:** On Wednesday, May 27, 2015, the NSABP B-52 study was temporarily suspended to accrual.

NRG realizes that some patients who have consented to participate in the study may not have completed their pre-entry biopsy to obtain fresh tumor samples by May 27; therefore, patients who have signed the B-52 consent form on or before May 27, 2015, will be permitted to enter.

**NRG-LU001:** Amendment 1, version date: May 7, 2015 ICF changes include:
“Changes in taste” and “changes in vision” were moved from the “rare and serious” column to the “occasional, some may be serious” column to be consistent with CTEP’s March 24, 2015 risk profile.

A NOTE TO PARTICIPATING SITES was added for clarity, and “You may need to pay for metformin HCL” was deleted, to further highlight that metformin may not be covered by patient insurance and to clarify sites’ option to either cover metformin costs or require patients to cover those costs.

**RTOG 0924:** The quality of life component has been closed to accrual.

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**CTSU Update:**
Clinical Trials Reporting Program (CTRP) was established on June 15, 2015. NCI’s Clinical CTRP was established in response to a recommendation made by the NCI Clinical Trials Working Group (CTWG) to the National Cancer Advisory Board (NCAB), and reiterated by the Institute of Medicine’s (IOM) report titled A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program. CTRP is a comprehensive database of regularly updated information, including accrual, on all NCI-supported clinical trials. This database of the entire NCI portfolio will help identify gaps in clinical research and duplicative studies facilitate effective clinical trial prioritization and enhance patient accrual to trials by making physicians aware of relevant opportunities for participation in clinical trials.

The CIRB Operations Office has developed a Handbook for Local Institutions to introduce local institutions to the purpose and function of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) Initiative and provide information to guide the process of enrollment and utilization. The Handbook for Local Institutions is available on the CIRB website at www.ncicirb.org on the home page under What’s New. You can also locate the handbook by clicking on the How to Join tab and selecting Enrollment Packet.

**CIRB Updates Tab:** The Home Tab on the CTSU
NRG cont.  

**NSABP-B43 & B47: Overview of Amendment Changes**

Due to an update in the Trastuzumab Investigator’s Brochure (IB) (Version 15, October 2014), women of reproductive potential (randomized to Arm 2 for B-47) must now agree to use an effective non-hormonal method of contraception during therapy and until at least 7 months after completion of trastuzumab, instead of during therapy and until at least 6 months.

Expedited reporting via CTEP-AERS of pregnancy, fetal death, or death neonatal is required while the patient is receiving study therapy or within 7 months following the last dose of study therapy.

The length of time that patients should not become pregnant or breastfeed a baby while on this study has been changed to at least 7 months after the last dose of trastuzumab.

Consent Form Addendum #1 has been added to inform women of reproductive potential who have completed trastuzumab in the past 7 months, of the updated requirement for use of an effective non-hormonal method of contraception during therapy and for at least 7 months after completion of trastuzumab.

Instructions for informing patients

Due to updated information included in Consent Form Addendum #1, at a minimum, patients who are of child-bearing potential (randomized to Arm 2 for B-47) and who are receiving or have completed trastuzumab in the last 7 months need to be informed of the information presented in Consent Form Addendum #1. Follow your local IRB policies and procedures regarding whether additional patients need to be informed.

Sites with patients who meet the criteria to be presented with the new information in Consent Form Addendum #1 will be provided with a list of patients by US Mail. The list will be sent to the Contact PI and NRG Lead RA for the site. If a patient on the list is no longer of child-bearing potential then document the reason why she did not need to sign the Consent Form Addendum in the patient’s research record.

**ECOG-ACRIN Update:**

**ECOG-ACRIN Upcoming Performance Monitoring:** The next Performance Monitoring data cut-off date of *June 30, 2015* is approaching. Any data received on or before June 30, 2015 will be included in the upcoming Performance Monitoring. Data received after June 30, 2015 will be considered late. It is important to remember that data timeliness will be evaluated by assessing two components: The rate of CRF submitted and the rate of survival follow-up. To avoid penalties, each evaluable ECOG-ACRIN institution must have a score of 90% or better on each component.

**Protocol Notice: E2511, Phase I and Randomized Phase II Double Blind Clinical Trial of Cisplatin and Etoposide in Combination with Veliparib (ABT-888) or Placebo as Frontline Therapy for Extensive Stage Small Cell Lung Cancer,** will close to accrual on *July 2, 2015*. The study is approaching its national accrual goal. Patients currently on study may continue on treatment. Patients enrolled on the study should continue to be followed per protocol. Thank you to all who participated in this trial.

**PRE-ACTIVATION OF PROTOCOL EAY131, Molecular Analysis for Therapy Choice (MATCH) Notice:** EAY131 has been reviewed Protocol and approved by the NCI Central Institutional Review Board (CIRB), and only sites utilizing the CIRB as their IRB of record will be able to participate in the trial. The phase II NCI-MATCH trial will incorporate more than 20 different study drugs or drug combinations, each targeting a specific gene mutation, in order to match each patient in the trial with a therapy that targets a molecular abnormality in their tumor. Each patient will initially enroll for screening, during which samples of their tumor will be biopsied and sequenced to detect genetic abnormalities that may be driving tumor growth and might be targeted by one of a wide range of drugs being studied. If a molecular abnormality is detected for which there is a sub-study available, patients will be further evaluated to determine if they meet the specific eligibility requirements within that...
MATCH cont.

arm. Once enrolled, patients will be treated with the targeted drug regimen for as long as their tumor shrinks or remains stable. Trial investigators plan to screen at least 3,000 patients during the full course of the trial with the goal of enrolling approximately 1,000 patients in the various treatment arms (with up to 35 patients each). The trial’s design calls for at least one-quarter of the enrolled patients to have rare cancers (defined as cancers other than non-small cell lung, prostate, breast, or colon cancers).

Participants must be age 18 or older, with solid tumors or lymphomas that have advanced following at least one line of standard systemic therapy, or with tumors for which there is no standard treatment.

Two endpoints will be evaluated: overall response rate (ORR; primary endpoint) and 6-month PFS (secondary endpoint). Within molecularly targeted subpopulations, an ORR of 16%-25% or higher and a 6-month PFS of 35% or higher will be considered promising results. NCI-MATCH is a “highly coordinated effort,” study co-chair Barbara A. Conley, MD, of NCI, said. The study was co-developed by NCI and the ECOG-ACRIN Cancer Research Group, is part of the NCI-sponsored National Clinical Trials Network (NCTN), and is being led by ECOG-ACRIN. The principal investigators who will lead the sub-studies are situated throughout the NCTN and its participating network groups: ECOG-ACRIN, the Alliance for Clinical Trials in Oncology, NRG Oncology, and SWOG. Patient advocates were engaged in the development of the trial and will help oversee the protocol and other aspects of the study.

Upcoming Events:

NRG Semi-Annual Meeting:
Denver CO, July 16th-19th
CRA Meeting: Virtual Meeting, September 30th
JOG Investigators Meeting: King of Prussia PA, October 15th
ECOG-ACRIN Semi-Annual Meeting: Orlando FL, November 12th-14th
CRA Meeting: Jefferson Campus, December 16th

The Clinical Research E-News Archive is now located on the Sidney Kimmel Cancer Center webpage under the JKCCN Member Area:
http://www.kimmelcancercenter.org/jkccn/e-newsletters.html

Sidney Kimmel Cancer Network Homepage:
http://www.kimmelcancercenter.org/jkccn/. This page contains links to the Remote Access Portal as well as the clinical trial document repository.

Contact Information:

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For urgent clinical trial questions or assistance please page: 877-656-9004