Newton-Wellesley Hospital's

Oncology Research News

Newsletter from the Office of Research ■ Winter 2010-11

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Content:

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AAHRPP
Enhancing Protections for Research Participants

AAHRPP offers accreditation to research organizations that provide comprehensive protections to research participants.

AAHRPP Reaccreditation Site Visit

The Association for the Accreditation of Human Research Protection Programs conducted a Reaccreditation Site Visit at Newton-Wellesley Hospital on October 26 and 27. During the two day visit, the Site Visitors interviewed 32 people including research leadership, IRB members, Investigators, Study Coordinators, Pharmacists, and research colleagues from Partners. The site visit went very well. We would like to thank all of you who participated.

NWH received a report with the results of the site visit on November 4, 2010. The Site Visitors were very complimentary of our Human Research Protection Program (HRPP) and specifically mentioned the following strengths:

- The Organizational Official, The Manager of the Office of Research, and the Human Research and Investigation Committee Chair were accessible and maintained a hands-on approach in carrying out their responsibilities.
- There was a strong network of relationships between the various components of the NWH Human Research Protection Program (HRPP) and the Partners HRPP.
- The HRPP optimized the resources available to support the HRPP activities
- The HRPP had a strong program of continuous quality improvement

The report identified two minor areas of concern. Both of these areas have been addressed and a response was submitted to AAHRPP on December 1, 2010. Our application for reaccreditation, the site visit report and our response will be reviewed by the Council on Accreditation in March 2011.

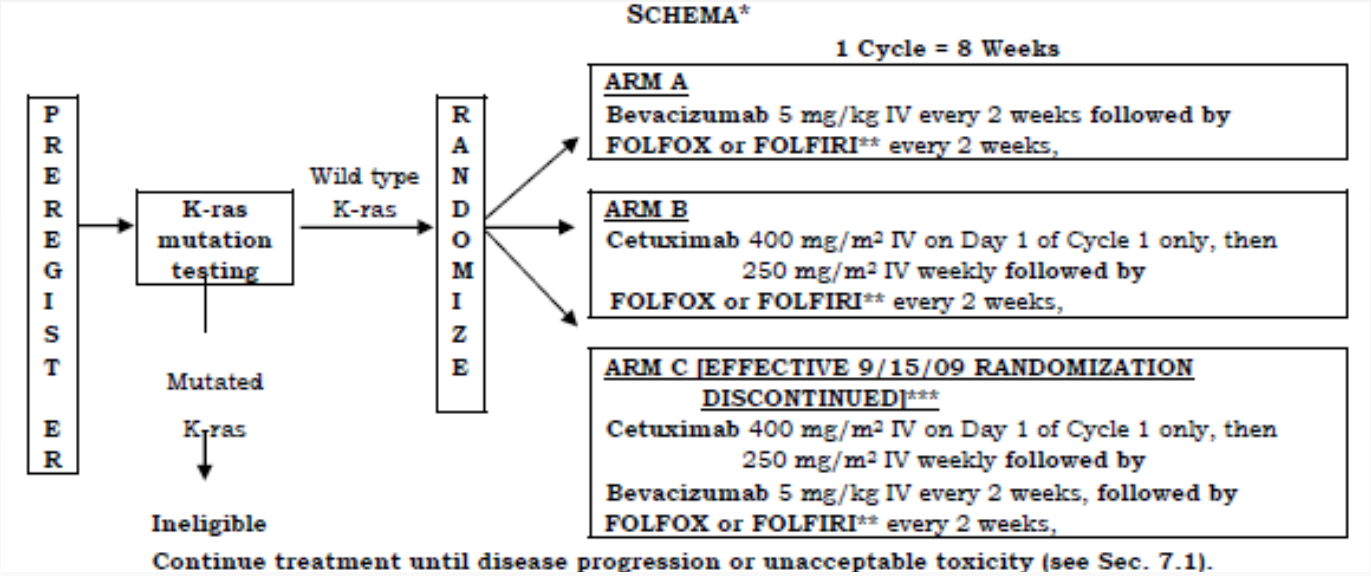
Submitted by: Hope Violette, Manager, Office of Research

Oncology Research News is published quarterly by the Newton-Wellesley Hospital Office of Research and distributed via NWH email. Forward suggestions and correspondence to Judy Chow jgchow@partners.org.

Newly Approved Trial

C80405

A Phase III Trial of Irinotecan / 5-FU / Leucovorin or Oxaliplatin / 5-FU / Leucovorin with Bevacizumab, or Cetuximab (C225) for Patients with Untreated Metastatic Adenocarcinoma of the Colon or Rectum



Patient Eligibility

- Histologically or cytologically documented locally advanced or metastatic adenocarcinoma of the colon or rectum (see Sec. 4.1)
- Only patients with a wildtype K-ras gene are eligible (see ⊏ 4.2)
- No prior systemic treatment for advanced or metastatic colorectal cancer (see ⊏4.3.1)
- - No prior radiotherapy to > 25% of bone marrow (see ⊏4.3.2)
- ≥ 4 weeks since major surgery (see ⊏4.3.3)
- No previous or concurrent malignancy (see ⊏4.4)
- For FOLFIRI patients: No evidence of Gilbert's syndrome or of homozygosity for the UGT1A1*28 allele (see ⊏4.5)
- No ≥ grade 2 sensory peripheral neuropathy for FOLFOX patients
- No known central nervous system metastases or carcinomatous meningitis
- No interstitial pneumonia or extensive and symptomatic interstitial fibrosis of the lung
- No pleural effusion or ascites that causes ≥ grade 2 dyspnea
- No predisposing colonic or small bowel disorders in which the symptoms are uncontrolled (see ⊏4.10)
- No uncontrolled seizure disorder or active neurological disease
- No current congestive heart failure; hypertension must be well controlled (<160/90); and patients on fulldose anticoagulants must be on a stable dose of warfarin and have an in-range INR or be on a stable dose of LMW heparin (see ⊏4.12-14)
- No significant history of bleeding events or GI perforation; no recent (within 6 months) arterial thrombotic events; and no serious or non-healing wound, ulcer or bone fracture (see ⊏4.15-17)
- No known hypersensitivity to Chinese hamster ovary cell products or to recombinant human or murine antibodies (see ⊏4.18)
- Not pregnant and not nursing (see ⊏4.19)
- ECOG Performance Status: 0-1
- Age ≥ 18

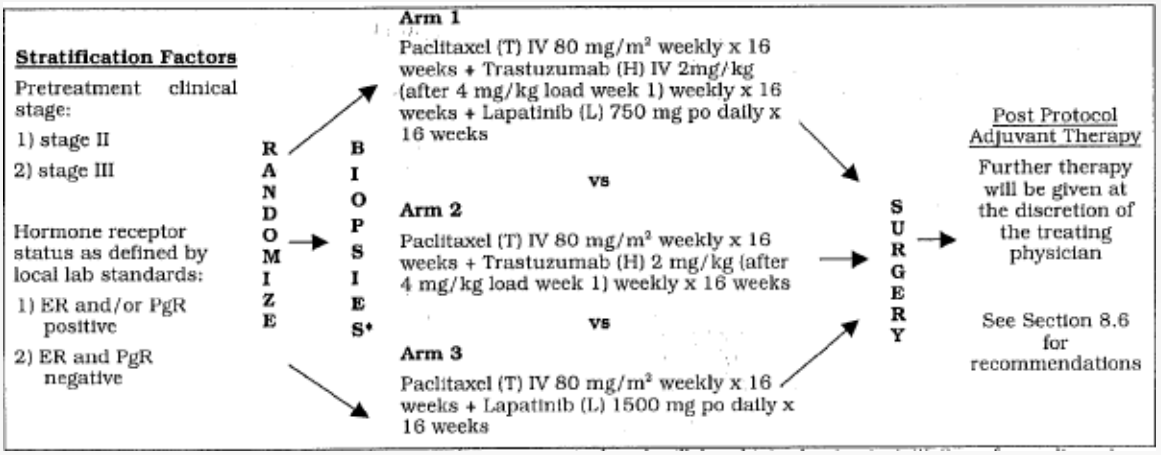
Source: www.calgb.org.C80405 Protocol Document Update 8/15/2010
https://www.calgb.org/Private/COOP_Groups/CALGB/studies/protocols/protocol_documents/gi/80405/80405-09.pdf

Newly Approved Trial

C40603

Randomized Phase II 2 X 2 Factorial Trial Of The Addition Of Carboplatin +/- Bevacizumab To Neoadjuvant Weekly Paclitaxel Followed By Dose dense AC In Hormone Receptor-Poor/Her2-Negative Resectable Breast Cancer.

DF# 09-260



Patient Eligibility

Please note: all lab tests must be completed within 16 days prior to study entry. Other non-lab tests must be performed within 4 weeks of study entry.

- Pathologic confirmation of invasive breast cancer (subjects with inflammatory breast cancer are not eligible)
- Clinical stage II-III invasive breast cancer with intent to perform surgical resection after neoadjuvant therapy. Staging to rule out metastatic disease is recommended for clinical stage III subjects
- Subjects with multicentric or bilateral disease are eligible as long as the target lesion meets the eligibility criteria for this study
- Tumors must be HER2 positive defined as HER2 3+ by immunohistochemical (IHC) assays or gene amplification by FISH with a ration of ≥ 2 on invasive tumor
- EG/PgR status must be known
- Target lesion in breast must be ≥ 1 cm on physical examination or by radiographic measurement.
- Subjects with axillary disease only are not eligible to participate
- Subject agrees to provide pretreatment biopsies
- No prior chemotherapy, hormone therapy, biologic or radiation therapy with therapeutic intent for this cancer.
- Cardiac ejection fraction ≥ 50% by echocardiogram or MUGA scan
- Age ≥ 18 years

Source: www.calgb.org.C40603 Protocol Document Update 12/1/2010
https://www.calgb.org/Private/COOP_Groups/CALGB/studies/protocols/protocol_documents/breast/40603/40603p.php

Recently Approved Studies

Cancer and Leukemia Group B (CALGB) TRIALS

CALGB 40502

For Women With Locally Recurrent or Metastatic Breast Cancer

CALGB 40502 available through DF/PCC Affiliation

Randomized phase III trial of weekly paclitaxel compared to weekly nanoparticle albumin bound nab-paclitaxel or ixabepilone, all combined with bevacizumab, as first -line therapy for locally recurrent or metastatic breast cancer

Treatment Plan

Patients will be randomized with equal probability to receive one of three treatment arms described below. Protocol therapy will be administered weekly for three weeks followed by one week of rest. Treatment cycle = 28 days.

Arm A: Weekly paclitaxel + bevacizumab

Paclitaxel 90 mg/m² IV infusion over one hour on days 1, 8, and 15 each cycle.
Bevacizumab 10mg/kg following paclitaxel treatment on days 1 and 15 of each cycle.

Arm B: Weekly nab-paclitaxel + bevacizumab

Nab-paclitaxel 150 mg/m² IV infusion over 30 minutes on days 1, 8, and 15 each cycle.
Bevacizumab 10 mg/kg following nab-paclitaxel treatment on days 1 and 15 of each cycle.

Arm C: Weekly Ixabepilone + bevacizumab

Ixabepilone 16 mg/m² IV infusion over 60 minutes on days 1, 8, and 15 each cycle.
Bevacizumab 10 mg/kg following ixabepilone treatment on days 1 and 15 of each cycle.

CALGB 40601

For Women with HER-2 Positive Primary Breast Cancer

CALGB 40601 Available Through CTSU

Randomized Phase III Trial Of Paclitaxel Combined With Trastuzumab, Lapatinib, Or Both As Neoadjuvant Treatment Of Her2-Positive Primary Breast Cancer.

Treatment Plan

Patients will be randomized to receive weekly paclitaxel with either trastuzumab weekly, or lapatinib daily or both administered for a total of 16 weeks.

Neoadjuvant Therapy:

Arm I: (THL)
Trastuzumab 2mg/kg IV weekly for 16 weeks plus
Paclitaxel 80 mg/m² IV weekly for 16 weeks plus
Lapatinib 750 mg PO daily for 16 weeks

Arm II: (TH)
Trastuzumab 2mg/kg IV weekly for 16 weeks plus
Paclitaxel 80 mg/m² IV weekly for 16 weeks

Arm III: (TL)
Paclitaxel 80 mg/m² IV weekly for 16 weeks plus
Lapatinib 1500 mg PO daily for 16 weeks.

For questions regarding clinical trials contact Kara Malcolm 617-243-5089 kmalcolm@partners.org

***Source*: Cancer and Leukemia Group B** website: www.calgb.org Central Office 230 W. Monroe Street Suite 2050 Chicago, IL 60606-4703 (773) 702-9171.

Partners in Excellence

Congratulations to Newton-Wellesley's 2010 Partners in Excellence Award recipients!

Individual Award:

Taryn Rourke, Genetic Counselor at the Vernon Cancer Center

Team Award:
Vernon Cancer Center Implementation Team
Team Leaders: Monique Porter & Julie Breakey

This is Newton-Wellesley Hospital's 12th year participating in the annual Partners in Excellence Awards Program!

The program is designed to spotlight and thank those individuals and teams whose high standards inspire each of us and enable NWH to provide the highest level of care to our community. Nominations were based on accomplishments "above and beyond the call of duty" in the following award categories: quality treatment and service, leadership and innovation, teamwork, operational efficiency and outstanding community contributions.

Dana-Farber/Partners Cancer Care
Affiliate Network Trials

Risk Evaluation And Cancer History Questionnaire

Breast and Ovarian Cancer Risk and Prevention

Research Studies

REACH: Risk Evaluation & Cancer History

Why is this study being done?

The REACH project collects risk factor information, blood and tissue specimens from patients and family members at high risk for breast and/or ovarian cancer. The data and specimen bank will be used as a resource to be shared with researchers working in the areas of breast and ovarian cancer risk, prevention and treatment.

Who is eligible to participate?

Individuals with an increased risk of breast cancer are eligible. Subjects are eligible to join the study if they meet any of the following criteria:

Personal or family history of breast cancer and/or ovarian cancer associated with at least a 20 percent chance of having a mutation in one of the known "breast cancer" genes.

Subject, or close family member, have a mutation in one of the known genes associated with increased cancer risk (BRCA1, BRCA2, p53, chk2, PTEN).

How long is the study?

One-time, approximately 30 minutes to fill out the questionnaire and have blood drawn.

What is involved?

Subjects will be asked to complete a questionnaire and a Family History Form

Subjects will be asked to donate three tubes of blood (approximately six tablespoons) for use in research.

***Source*: http://www.dana-farber.org/pat/cancer/breast-ovarian/reach.html**
Dana-Farber Cancer Institute 44 Binney Street Boston, MA 02115 Research Studies on Breast and Ovarian Cancer Risk & Prevention

Study Highlights

CALGB 40502

Regulatory Reminder

CITI Collaborative Institutional Training Initiative
www.citiprogram.org

All investigators and research personnel participating in the conduct of human-subject research must complete the basic education program developed by the Collaborative Institutional Training Initiative (CITI).

The CITI program is comprehensive and provides case-based learning of ethical concepts and regulations in a web-based learning environment.

The **Basic Course** (for new personnel) is the first course to complete.

Once you have completed the **Basic Course**, all researchers and their staff are required to complete the CITI **Refresher Course** every three years.

For Women with Locally Recurrent or Metastatic Breast Cancer

CALGB 40502 Available Through the CTSU

A Randomized Phase III Trial of Weekly Paclitaxel Compared to Weekly Nanoparticle Albumin Bound Nab-Paclitaxel or Ixabepilone Combined with Bevacizumab as First-Line Therapy for Locally Recurrent or Metastatic Breast Cancer

Patient Population

See Section 4 for Complete Eligibility Details

- Patients must have histologic confirmation of invasive Stage IV or Stage IIIC breast cancer not amenable to local therapy.
- Patients must have measurable disease.
- Patients must *not* have any concurrent active secondary malignancy.
- Patients may have HER2 negative disease, or HER2+ disease if prior trastuzumab or lapatinib therapy was received.
- Patients must have known ER/PgR status at the time of study registration.
- Patients may have been treated previously with adjuvant or neoadjuvant taxane *(with ≥12 months between completion of therapy and progression)*, radiation therapy *(completed ≥ 2 weeks prior to study entry)*, hormonal therapy *(last dose administered ≥ 7 days prior to initiation of protocol therapy)*.
- Patients may be receiving bisphosphonates and may have received prior bevacizumab.
- Patients must *not* have had prior chemotherapy for metastatic breast cancer.
- Patients must *not* have had major surgery ≤ 28 days prior to registration.
- Patients must have ECOG (Zubrod) PS of ≤1 and a life expectancy of ≥12 weeks.
- Patients must *not* have a history of CTCAE ≥ grade 3 hypersensitivity to paclitaxel or Cremophor EL.
- Patients must *not* have progressing or untreated CNS metastases or leptomeningeal disease.

Treatment Plan

See Section 8 for Complete Treatment Plan Details

Protocol treatment is to begin within 14 days of registration. A treatment cycle is defined as 28 days.

Arm A: Weekly paclitaxel* + bevacizumab
- Paclitaxel 90 mg/m² IV infusion over 1 hour on days 1, 8, 15 of each cycle
- Bevacizumab 10 mg/kg following paclitaxel treatment on days 1 and 15 of each cycle

Arm B: Weekly nab-paclitaxel + bevacizumab
- Nab-paclitaxel 150 mg/m² IV infusion over 30 minutes on days 1, 8 and 15 of each cycle
- Bevacizumab 10 mg/kg following nab-paclitaxel treatment on days 1 and 15 of each cycle

Arm C: Weekly ixabepilone** + bevacizumab
- Ixabepilone 16 mg/m² IV infusion over 60 minutes on days 1, 8 and 15 of each cycle
- Bevacizumab 10 mg/kg following ixabepilone treatment on days 1 and 15 of each cycle

*See section 8.1 for details regarding premedication for paclitaxel (recommended for initial dose and may be altered at discretion of treating physician).

**See section 8.3 for details regarding premedication for ixabepilone.

For questions regarding clinical trials contact
Kara Malcolm 617-243-5089 kmalcolm@partners.org

Please Enroll Your Eligible Patients!

Work In Progress

AWAITING DF IRB APPROVAL

NON SMALL CELL LUNG

NSCLC: 08-144/30704: 2nd line NSCLC
Pemetrexed vs. sunitinib vs. both

LYMPHOMA

Mantle cell lymphoma, relapse/refractory: 08-066/50501:
Bortezemib and lenalidomide (ph II)

REQUESTING TRIAL TO BE OPENED AT NWH/NEHO

NON SMALL CELL LUNG

NSCLC: 07-338/1505 – adjuvant stages IB-IIIA
Cisplatin-containing chemo (MD choice) +/- bevacizumab *(enrollment on hold per BIDMC)*

RENAL

09-173: mechanisms of hypertension and proteinuria in patients treated with anti-angiogenesis chemotherapy

COLON

Colon: 06-042/5202 – adjuvant, high risk stage II
5FU/Leucovorin/oxaliplatin +/- bevacizumab

CURRENTLY UNDER IRB REVIEW AT DF/PCC (enrollment on hold per BIDMC)

MGH PATHOLOGY Study

Pathologist face-to-face patient consults to review path slides
Will start with selected breast center patients

CALGB Breast Cancer Studies with Bevacizumab: Update 12.10 – Winer & Hudis

Given the recent decision of the FDA to withdraw accelerated approval, CALGB 40502 will be amended in protocol Update #4 to allow, but not require, use of bevacizumab in combination with chemotherapy. The use of bevacizumab will then be optional for patients enrolled after the amendment has received IRB approval at local IRBs.

The decision as to whether the patient will receive bevacizumab must be declared at the time of registration, and bevacizumab will continue to be provided by CTEP for patients electing to receive this agent.

Patients already enrolled in this trial will continue to receive bevacizumab, and should follow study guidelines regarding management of toxicity and discontinuation of therapy.

The decision to make this change in the protocol is to allow maximum flexibility for patients enrolling in the trial, keeping in mind both the benefits seen with bevacizumab in the first-line trials as well as the recent FDA decision.

***Source*: January 2011 Research Update presentation at New England Hematology/Oncology Associates Provider's Meeting 1/3/2011. Caroline C. Block, M.D. Associate Clinical Professor of Medicine Tufts University School of Medicine cblock@partners.org**