CALGB 40502/NCCTG N063H/CTSU 40502

A Randomized Phase III Trial of Weekly Paclitaxel Compared to Weekly Nanoparticle Albumin Bound Nab-paclitaxel or Ixabepilone With or Without Bevacizumab as First-Line Therapy for Locally Recurrent or Metastatic Breast Cancer

ClinicalTrial.gov Identifier: NCT00785291

Study Background

Trial Description

This randomized phase III trial studies the side effects and how well different chemotherapy regimens with or without bevacizumab work in treating patients with stage IIIC or stage IV breast cancer. Drugs used in chemotherapy, such as paclitaxel, paclitaxel albumin-stabilized nanoparticle formulation (nab-paclitaxel), and ixabepilone, work in different ways to stop the growth of tumor cells, either by killing the cells, by stopping them from dividing, or by stopping them from spreading. Bevacizumab may block tumor growth by targeting certain cells and slowing the growth of blood vessels to the tumor. It is not yet known which treatment regimen is more effective in treating patients with breast cancer.

Arms:

Arm A (Paclitaxel): (Active Comparator): Patients receive 90 mg/m^2 paclitaxel IV over 1 hour on days 1, 8, and 15. Patients may receive 10 mg/kg bevacizumab IV over 30-90 minutes on days 1 and 15.

Arm B (Nab-paclitaxel): (Experimental): Patients receive paclitaxel albumin-stabilized nanoparticle formulation IV over 30 minutes on days 1, 8, and 15. Patients may also receive 10 mg/kg bevacizumab IV over 30-90 minutes on days 1 and 15.

Arm C (Ixabepilone): (Experimental): Patients receive ixabepilone IV over 60 minutes on days 1, 8, and 15. Patients may also receive 10 mg/kg bevacizumab IV over 30-90 minutes on days 1 and 15. (closed to accrual as of 7/18/11)

Objectives:

- PRIMARY OBJECTIVES:
- I. To compare the progression-free survival (PFS) in patients with metastatic breast cancer receiving nab-paclitaxel versus paclitaxel (control arm).

II. To compare PFS in patients receiving ixabepilone versus paclitaxel.

- SECONDARY OBJECTIVES:
- I. To compare the objective response rate, duration of response, and time to treatment failure in patients receiving nab-paclitaxel versus paclitaxel, and to separately compare these endpoints in patients receiving ixabepilone versus paclitaxel.
    III. To compare the 12-month rate of progression in patients receiving nab-paclitaxel versus paclitaxel, and to separately compare this endpoint in patients receiving ixabepilone versus paclitaxel.
    III. To determine toxicities in patients receiving nab-paclitaxel as compared to paclitaxel, and in patients receiving ixabepilone as compared to paclitaxel.
    IV. To compare overall survival in patients receiving nab-paclitaxel versus paclitaxel, and to separately compare overall survival in patients receiving ixabepilone versus paclitaxel.
- V. To evaluate the relationships between secreted protein, acidic, cysteine-rich (SPARC) overexpression and changes in blood levels of caveolin-1 (Cav-1) to PFS and secondary endpoints of response during treatment with nab-paclitaxel as compared to paclitaxel, and with ixabepilone as compared to paclitaxel.

    VI. To evaluate the relationships between changes in blood levels of circulating tumor cells (CTCs) and circulating endothelial cells (CECs) to PFS and secondary endpoints of response during treatment with nab-paclitaxel as compared to paclitaxel, and with ixabepilone as compared to paclitaxel.
    VII. To evaluate the association of expression levels of the microtubule associated proteins tau and beta-tubulin isotype composition with PFS and secondary endpoints of response during treatment with nab-paclitaxel as compared to paclitaxel, and with ixabepilone as compared to paclitaxel.
    VIII. To investigate a potential cytochrome P450, family 2, subfamily C polypeptide 8, 2, 3(CYP2C8*2/*3) by paclitaxel interaction with respect to progression-free survival (PFS).
    IX. To determine if CYP2C8*2 and CPY2C8*3 are associated with paclitaxel-induced peripheral neuropathy.
- X. To perform exploratory analysis of cytochrome P450, family 3, subfamily A, polypeptide 4 (CYP3A4), cytochrome P450, family 3, subfamily A, polypeptide 5 (CYP3A5), ATP-binding cassette, sub-family B (MDR/TAP), member 1 (ABCB1) and ATP-binding cassette, sub-family C (CFTR/MRP), member 2 (ABCC2) polymorphisms with response and toxicity profiles.
    XI. To prospectively collect data on socio-demographics, non-cancer morbidities, and receipt of post-trial therapy to evaluate the role of potential disparities on survival from cancer.
    XII. To evaluate the relationship between physical activity behaviors at the time of enrollment in the protocol and progression-free and overall survival.
    XIII. To identify baseline factors that predict the risk of grade 3, 4, or 5 toxicity in patients receiving treatment with weekly paclitaxel, nab-paclitaxel, or ixabepilone combined with or without bevacizumab.

XIV. To perform an exploratory analysis of whether other factors included in patient assessments (either individually or in combination) predict the risk of grade 3, 4, or 5 toxicity in patients receiving weekly paclitaxel, nab-paclitaxel, or ixabepilone combined with or without bevacizumab, with a specific focus on the relationship between pre-existing hypertension or neuropathy.

XV. To compare the associations of baseline factors to grade 3, 4, or 5 toxicity in patients receiving weekly paclitaxel, nab-paclitaxel, or ixabepilone combined with or without bevacizumab.

XVI. To explore whether longitudinal changes in factors are in association with the occurrence of grade 3, 4, or 5 toxicities in patients with weekly paclitaxel, nab-paclitaxel, or ixabepilone combined with or without bevacizumab.

XVII. To explore the association between grade 2-4 neuropathy and longitudinal changes in the following functional status measures: a) Older Americans Resources and Services (OARS) Multidimensional Functional Assessment Questionnaire (MFAQ) (Instrumental Activities of Daily Living [IADL]); b) Medical Outcomes Study (MOS) Physical Functioning; c) Karnofsky Performance Status Rated Healthcare Professional; d) Timed "Up and Go"; e) OARS Physical Health Section.

- OUTLINE: Patients are randomized to 1 of 3 treatment arms.
- In all arms, treatment repeats every 28 days in the absence of disease progression or unacceptable toxicity.
- After completion of study therapy, patients are followed every 6 months for 2 years and then annually for up to 3 years.

Study Milestones:

Start date: October 2008

Primary Completion Date: December 31, 2013

Publication Information:

Analysis Type: Primary

Pubmed ID: 26056183

Citation: J Clin Oncol. 2015 Jul 20;33(21):2361-9. doi: 10.1200/JCO.2014.59.5298. Epub 2015 Jun 8.

Associated Datasets: NCT00785291-D1-Dataset.csv (c40502_ae_all), NCT00785291-D2-Dataset.csv (c40502_cycles_all), NCT00785291-D3-Dataset.csv (c40502_efficacy_all)

Dataset Information:

Dataset Name: NCT00785291-D1-Dataset.csv (c40502_ae_all)

Description: Dataset NCT00785291-D1-Dataset.csv (c40502_ae_all) is one of 3 datasets associated with PubMed ID 26056183. This dataset contains one record per adverse event (AE) per patient for those who began treatment.

Data can be used to approximate published study findings, but exact reproduction of previous manuscripts may not be possible in some cases (e.g., when data must be modified for de-identification purposes or have undergone further data cleaning).

Blank values indicate data not applicable or missing except where otherwise noted.

NCT00785291-D1-Dataset.csv (c40502_ae_all) Data Dictionary:

LABEL	NAME	elements	comments
Was an AER submitted?	AER_submitted	1=Yes, 2=No, MISSING=N/A	
AE meddra code	meddra_code		
Version of CTC used	CTC_version	3, 2	
Version of meddra used	meddra_version	6, 5	
Grade of AE reported	grade_ID	0=None, 1=Mild, 2=Moderate, 3=Severe, 4=Life-threatening, 5=Fatal	
Treatment attribution	relation_ID	MISSING=Missing, 0=Unknown, 1=Unrelated, 2=Unlikely, 3=Possible, 4=Probable, 5=Definite	
Category of AE	category		

AE name	eventname		
Specify comment	specify		
Option selected	select_AE		
Patient identifier	patid		