CALGB-40601

Randomized Phase III Trial of Paclitaxel +Trastuzumab + Lapatinib Versus Paclitaxel + Trastuzumab as Neoadjuvant Treatment of HER2-Positive Primary Breast Cancer

ClinicalTrial.gov Identifier: NCT00770809

Study Background

Trial Description

This randomized phase III trial studies paclitaxel and trastuzumab with or without lapatinib to see how well they work in treating patients with stage II or stage III breast cancer that can be removed by surgery. Drugs used in chemotherapy, such as paclitaxel, 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. Monoclonal antibodies, such as trastuzumab, can block tumor growth in different ways. Some block the ability of tumor cells to grow and spread. Others find tumor cells and help kill them or carry tumor-killing substances to them. Lapatinib may stop the growth of tumor cells by blocking some of the enzymes needed for cell growth. Giving paclitaxel with trastuzumab and/or lapatinib before surgery may make the tumor smaller and reduce the amount of normal tissue that needs to be removed. It is not yet known which regimen is more effective in treating patients with breast cancer.

Arms:

Arm I (THL): (Experimental): Patients receive trastuzumab 2 mg/kg IV over 30-90 minutes and paclitaxel 80 mg/m^2 IV over 1 hour once weekly and lapatinib ditosylate 750 mg PO once daily for 16 weeks in the absence of disease progression or unacceptable toxicity.

Arm II (TH): (Active Comparator): Patients receive trastuzumab 2 mg/kg IV over 30-90 minutes and paclitaxel 80 mg/m^2 IV over 1 hour once weekly for 16 weeks in the absence of disease progression or unacceptable toxicity.

Arm III (TL): (Experimental): Patients receive paclitaxel 80 mg/m^2 IV over 1 hour once weekly and lapatinib ditosylate 15000 mg PO once daily for 16 weeks in the absence of disease progression or unacceptable toxicity. (Discontinued as of 6-15-11)

Objectives:

PRIMARY OBJECTIVE:

I. To determine if the pathologic complete response (pCR) in the breast to neoadjuvant weekly paclitaxel with trastuzumab plus lapatinib (THL) is 20% greater than the pCR to weekly paclitaxel with trastuzumab alone (TH).

SECONDARY OBJECTIVES:

I. To determine the pathologic complete response in the breast and axilla, using American Joint Committee on Cancer (AJCC) Tumor, Lymph Nodes and Metastasis (TMN) criteria (version 6), to neoadjuvant weekly paclitaxel plus human epidermal growth factor 2 (HER2)- targeted therapy in patients with HER2-positive operable breast cancer.

II. To evaluate residual cancer burden (RCB) as a predictor of long term relapse free survival (RFS) and overall survival (OS).

III. To document the toxicity of all chemotherapeutic regimens (THL, TH).

IV. To determine the correlation between clinical, radiographic and pathologic response.

V. To compare overall survival (OS), relapse free survival (RFS) and time to first failure (TFF) among the treatment groups.

VI. To obtain blood, fresh frozen and fixed tumor tissue to test specific hypotheses for which biomarker data exist and to evaluate biomarkers in blood, serum and tissue that are likely to influence response to and toxicity of trastuzumab alone or trastuzumab plus lapatinib, when given with paclitaxel.

VII. To determine the surgical practice patterns for breast conservation and sentinel lymphadenectomy in patients undergoing neoadjuvant chemotherapy.

VIII. To determine the radiotherapy practice patterns for post-mastectomy and regional nodal irradiation in patients undergoing neoadjuvant chemotherapy.

IX. To evaluate pharmacogenomic determinants of toxicity.

OUTLINE: Patients are randomized to 1 of 3 treatment arms.

Study Milestones:

Primary Completion Date: January 31, 2014

Publication Information:

Analysis Type: Primary

Pubmed ID: 26527775

Citation: J. Clin. Oncol vol 34 (6) 542-549 2016

Associated Datasets:

NCT00770809-D1-Dataset.csv (consort),

NCT00770809-D2-Dataset.csv (consort_genetic),

NCT00770809-D3-Dataset.csv (table1),

NCT00770809-D4-Dataset.csv (fig3),

NCT00770809-D5-Dataset.csv (delay),

NCT00770809-D6-Dataset.csv (aeclean)

NCT00770809-D7-Dataset.csv (gene)

Dataset Information:

Dataset Name: NCT00770809-D6-Dataset.csv (aeclean)

Description: Dataset NCT00770809-D6-Dataset.csv (aeclean) is one of 7 datasets associated with PubMed ID 26527775. This dataset contains information on all the adverse events reported during each cycle while on trial. Therefore, patients can report the same adverse event over multiple courses of 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.

NCT00770809-D6-Dataset.csv (aeclean) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
PATIENT_ID	PATID		
MEDDRA_CODE	MEDDRA_CODE		
GRADE_ID	GRADE_ID	0, 1, 2, 3, 4, 5	
RELATION_ID	RELATION_ID	0=Unknown, 1= Not related to treatment, 2 = Unlikely related, 3 = Possibly related, 4= Probably related, 5 = Definitely related	Missing indicates either a grade zero was reported or a grade was assigned and no attribution was assigned.
The name of the adverse event recorded	EventName		
The category for each adverse event	EventCat		