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-D2-Dataset.csv (consort_genetic)

Description: Dataset NCT00770809-D2-Dataset.csv (consort_genetic) is one of 7 datasets associated with PubMed ID 26527775. This dataset contains information that will allow you to reproduce the Genomic analysis section of the consort diagram (including the patients used in the pre-Rx and pre- v post- genomic analysis). This data set includes the n=295 patients evaluable for efficacy.

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-D2-Dataset.csv (consort_genetic) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
PATIENT_ID	PATID		
Was the patient included in the genomic analysis pre-Rx?	genomic_pre	1= “Included in the Genomic analysis pre-Rx”, 0= “not included”	There were 265 patients used in the genomic analysis pre-Rx.
Was the patient included in the genomic analysis pre- v post-Rx?	pre_v_post	1=”Included in the genomic analysis pre- v post-Rx”, 0=”Patient not included”	Missing indicates the patient was not included in the pre_v_post analysis because they were not included in the pre-Rx analysis.
	pre_v_post_reas	Achieved pCR, No specimen, Normal-like	Only filled out where pre_v_post = 0 and if the patient was part of the pre-Rx analysis.
	pre_reas	Array QC failure, No pre-Rx specimen, Withdrew Consent	Missing indicates the patient was included in the pre-Rx analysis.