CALGB-40601

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

ClinicalTrials.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.
  - ARM I: Patients receive trastuzumab IV over 30-90 minutes and paclitaxel IV over 1 hour once weekly and lapatinib ditosylate orally (PO) once daily for 16 weeks in the absence of disease progression or unacceptable toxicity.
  - ARM II: Patients receive trastuzumab and paclitaxel as in arm I.
  - ARM III: Patients receive paclitaxel and lapatinib ditosylate as in arm I. (Discontinued as of 6-15-11) Within 42 days after completion of neoadjuvant therapy, patients in both arms undergo definitive surgery (breast conservation or total mastectomy). After completion of study treatment, patients are followed every 6 months for 2 years and then annually for up to 10 years.

Study Milestones:

Start Date: December 01, 2008

Primary Completion Date: January 31, 2014

Publication Information:

Analysis Type: Primary

PubMed ID: 33095682

Citation: Fernandez-Martinez A, Krop IE, Hillman DW, Polley MY, Parker JS, Huebner L, Hoadley KA, Shepherd J, Tolaney S, Henry NL, Dang C, Harris L, Berry D, Hahn O, Hudis C, Winer E, Partridge A, Perou CM, Carey LA. Survival, Pathologic Response, and Genomics in CALGB 40601 (Alliance), a Neoadjuvant Phase III Trial of Paclitaxel-Trastuzumab With or Without Lapatinib in HER2-Positive Breast Cancer. J Clin Oncol. 2020 Dec 10;38(35):4184-4193. doi: 10.1200/JCO.20.01276. Epub 2020 Oct 23. PMID: 33095682; PMCID: PMC7723687.

Associated Datasets: NCT00770809-D8-Dataset.csv (pts)

Dataset Information:

Dataset Name: NCT00770809-D8-Dataset.csv (pts)

Description: Dataset NCT00770809-D8-Dataset.csv (pts) is one of 1 datasets associated with PubMed ID 33095682. This dataset contains clinical data presented in the publication.

The RNAseq data has been submitted to GEO (Gene Expression Omnibus).

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-D8-Dataset.csv (pts) Data Dictionary:

LABEL	NAME	ELEMENTS	COMMENTS
Patient identifier	patid		
Intrinsic subtype	Subtype	Basal, Her2, LumA, LumB, NA, Normal	
RNA sequencing cohort	RNAseq_cohort	No, Yes	
Was adjuvant Adriamycin-cyclophosphamide received after the trial?	Adjuvant_AC	No, Yes	
Was adjuvant Trastuzumab completed?	Adjuvant_TTZ	No, Yes	
Pathologic Complete response in the breast	pCR_breast	NA, non_pCR, pCR	(yT0, yTis) & (ypN0, ypN0(i+)) w/d: withdrew. NA = Patients who withdrew consent prior to surgery were omitted from pCR analyses.
Treatment arm	Treatment_arm	TH, THL, TL	Corresponds to *indrx* in the D1 and D4 data submissions.
Age (years) at enrollment	ageatent		

LABEL	NAME	ELEMENTS	COMMENTS
Menopause status	meno	0=Premenopausal, 1=Postmenopausal	
Time to first event (event is either death by any cause or recurrence - local or distant) (years)	EFS_years		
Event free survival status (event is either death by any cause or recurrence - local or distant)	EFS_event	0=No event, 1=Event	
Survival time (years)	OS_time_years		
Race of participant	race	Black, Other, White	
Survival status (event is death)	OS_event	0=No event, 1=Event	
Stage	stra2_stage	1=Stage II, 2=Stage III	
Hormonal Receptor Status	stra3_recep	1=Positive, 2=Negative	
Performance status	PS	0, 1	