Alliance Public Study Result Summary
CALGB 40601

What this study is about

A breast cancer study that compared different drug treatments (chemotherapy) in patients with HER2 positive (HER2+) breast cancer that can be removed by surgery.

The full title of this study is: Randomized phase III trial of paclitaxel plus trastuzumab plus lapatinib versus paclitaxel plus trastuzumab or as neoadjuvant treatment of HER2-positive primary breast cancer

Why the study was done

There are different kinds of breast cancer. Some patients have too much of a cell marker called human epidermal growth factor receptor 2 (HER2). These patients are told they have HER2 positive breast cancer. Patients in this study had stage II or III HER2 positive breast cancer.

This study was done to see if a two-drug treatment called traztuzumab (common brand name herceptin) and lapatinib (common brand name tykerb) that targets HER2 positive breast cancer would make more breast cancer tumors go away, compared to a single drug treatment with traztuzumab by the time of surgery.

The study was also done to find out how whether two drugs made more cancer tumors go away before surgery. In addition, the study looked at any other issues that might be unique to the tumor's location.

Study results

Overall, there was no difference in what happened to patients, no matter which treatment group they were in.

The tumors were also studied to learn more about cell markers. It was found that cancer tumors responded differently to therapy, based on these cell markers:

- 7 out of 10 patients (70%) with HER2 positive had more tumors go away before surgery.
- In comparison, just over 3 out of 10 patients (35%) with HER2 negative cancers had more tumors go away before surgery.

There were also differences for some patients who had different levels of hormones called estrogen receptor (ER) and progesterone receptor (PR) that were in cancer cells:

- Patients whose cancer did not depend on ER or PR had more tumors go away before surgery. This is called ER negative and PR negative breast cancer.
- Patients whose cancer did depend on ER (ER positive) or PR (PR positive) had more tumors on scans that were taken before surgery.

Other factors that determined response included mutations in the *TP53* tumor suppressor gene and the expression of immune related genes.

What the results mean

This study was important because it showed that:

- Giving two drugs that target the HER2 receptor is not necessarily better than giving one.
- There are important differences among breast cancers that were not previously understand.
- Knowing about these differences and which ones are important will be critical to successfully tailor a patient's therapy and improve or predict response.

These results were unexpected and show that further studies are needed to determine the impact on response to therapy targeting HER2 in the future.

Alliance Public Study Result Summary
CALGB 40601

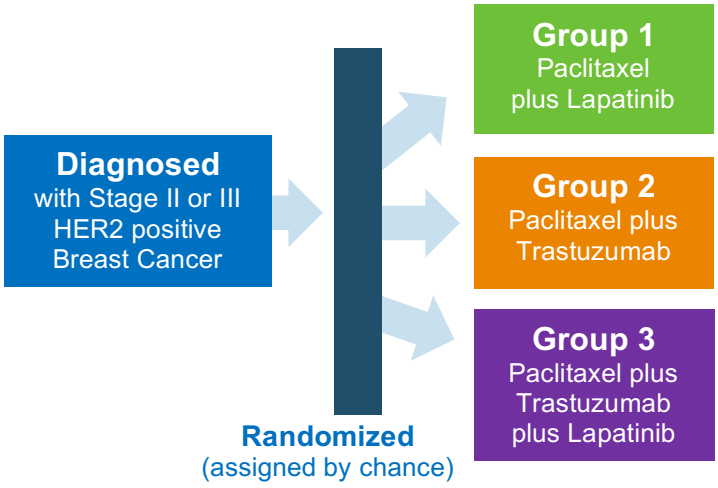
How the study worked

Patients with stage II or III HER2 positive breast cancer had a biopsy and were assigned by chance (randomized) to one of three groups.

All patients got chemotherapy (paclitaxel).

- One third of the patients (about 67 people) also got lapatinib that targeted the HER2 receptor, but that part of this study was closed early.
- One third of the patients (about 120 people) got trastuzumab that also targeted the HER2 receptor.
- One third of the patients (about 118 people) got both drugs (trastuzumab and lapatinib) that targeted the HER2 receptor.

Here is a picture that explains how patients were placed into this study.



When did the study start and end? The study started in December 2008. All patients were enrolled by February 2012.

How many patients joined? 305 patients agreed to be in this study.

Talk to your doctor if you want more information about this study.

Scientific publications about this study

This summary includes information in the following article:

- **Molecular Heterogeneity and Response to Neoadjuvant Human Epidermal Growth Factor Receptor 2 Targeting in CALGB 40601, a Randomized Phase III Trial of Paclitaxel Plus Trastuzumab With or Without Lapatinib.** Carey LA, Berry DA, Cirrincione CT, Barry WT, Pitcher BN, Harris LN, Ollila DW, Krop IE, Henry NL, Weckstein DJ, Anders CK, Singh B, Hoadley KA, Iglesia M, Cheang MC, Perou CM, Winer EP, Hudis CA. J Clin Oncol. 2016 Feb 20;34(6):542-9. doi: 10.1200/JCO.2015.62.1268. Epub 2015 Nov 2.

To learn about this trial, visit the ClinicalTrials.gov website at
https://clinicaltrials.gov/ct2/show/results/NCT00770809

Alliance Public Study Result Summary
CALGB 40601

This study was sponsored by the Alliance for Clinical Trials in Oncology – a national clinical trial network group that runs large cancer clinical trials. The Alliance is supported by the National Cancer Institute (NCI) and brings researchers together to develop better treatments for cancers. More information about the Alliance is at http://www.allianceforclinicaltrialsinoncology.org.

This summary lists what is known about this research study as of November 2015.
New Information may be available.

We thank the people who joined this study and made it possible.
We do research to try to learn the best ways to help patients.
The people who joined this study helped us to do that.

Thank you for your interest in learning more about cancer research advances.