Alliance Public Study Result Summary
NCCTG N063D

What this study is about

This study compared different drug treatments given after surgery for patients with HER2 positive breast cancer.

The full title of this study is: ALTTO (Adjuvant lapatinib and/or trastuzumab treatment optimisation study) - A randomised, multi-centre, open-label, phase III study of adjuvant lapatinib, trastuzumab, their sequence and their combination in patients with HER2/ErbB2 positive primary breast cancer

Why the study was done

The usual treatment of patients with HER2 positive breast cancer includes getting trastuzumab (common brand name herceptin) for one year.

This study was done to see if treatment with lapatinib (common brand name tykerb) could decrease the number of patients with HER2 positive breast cancer whose disease came back after surgery and chemotherapy.

In this study lapatinib was given in three different ways and was compared to not getting lapatinib.

Group 1: trastuzumab alone
Group 2: lapatinib alone
Group 3: trastuzumab followed by lapatinib
Group 4: trastuzumab and lapatinib together

Lapatinib is a pill. Trastuzumab is given by vein.

Study results

These results are for people with HER2 positive breast cancer of at least about a half inch in size and/or with positive lymph nodes who have already had surgery and are also getting chemotherapy.

During the study, patients getting lapatinib alone were doing worse than patients getting any treatment that contained trastuzumab. A safety monitoring committee noted this, and the study stopped putting patients in the lapatinib-only group. Patients already in the lapatinib alone group were notified and offered trastuzumab.

Adding lapatinib to trastuzumab in any order did not decrease the number of patients whose cancer came back. At the time the study was published, there was a small trend for fewer patients to have cancer came back in the group getting both drugs at the same time.

Adding lapatinib in any order did not change the number of patients alive four years after they were diagnosed. About 19 out of 20 patients who got trastuzumab and lapatinib in any order were alive four years after they were diagnosed.

Side effects from lapatinib included:

- Severe diarrhea: *10 out of 100 patients with lapatinib alone compared to 1 out of 100 patients with trastuzumab alone*
- Severe rash: *6 out of 100 patients with lapatinib alone versus 1 out of 100 patients with trastuzumab alone*
- Blood tests showing possible liver damage: *4 out of 100 patients with lapatinib alone versus 1 out of 100 patients with trastuzumab alone*

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What the results mean

This means that there was no benefit to lapatinib and patients getting lapatinib had worse side effects. Therefore, one year of trastuzumab without lapatinib remained the standard treatment for patients with HER2 positive breast cancer.

Longer follow-up was planned to see if results changed.

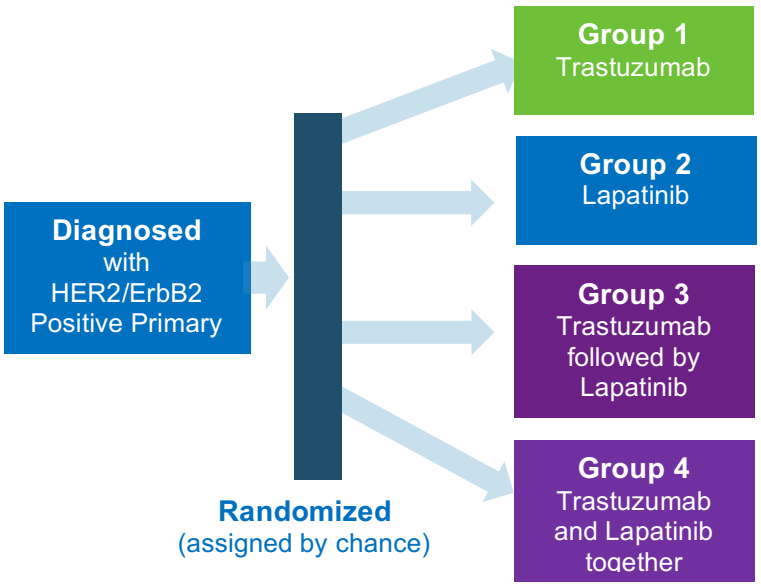
How the study worked

Patients with HER2 positive breast cancer who were able to join the study were assigned by chance (randomized) to one of four groups. This made sure that each patient had the same chance of being in any study group. One quarter of patients got just trastuzumab, one quarter got just lapatinib, one quarter got trastuzumab then lapatinib at different times, and one quarter got trastuzumab and lapatinib at the same time – all for one year.

All patients got chemotherapy. The order of treatments could be either all chemotherapy before any lapatinib and/or trastuzumab, or lapatinib and/or trastuzumab along with part of the chemotherapy. The patient and their physician decided the order of treatments.

Lapatinib was a pill taken daily; trastuzumab was given in the vein once a week during chemotherapy and every three weeks after chemotherapy treatments ended.

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



When did the study start and end? The study started in February 2008. All patients were enrolled by August 2011.

How many patients joined? 8,381 patients from 44 countries were enrolled on this study.

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

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Scientific publications about this study

This summary includes information in the following article:

- **Adjuvant Lapatinib and Trastuzumab for Early Human Epidermal Growth Factor Receptor 2-Positive Breast Cancer: Results from the Randomized Phase III Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization Trial.** Piccart-Gebhart M, Holmes E, Baselga J, de Azambuja E, Dueck AC, Viale G, Zujewski JA, Goldhirsch A, Armour A, Pritchard KI, McCullough, AE, Dolci S, McFadden E, Holmes AP, Tonghua L, Eidtmann H, Dinh P, Cosimo SD, Harbeck N, Tjulandin S, Im YH, Huang CS, Diéras V, Hillman DW, Wolff AC, Jackisch C, Lang I, Untch M, Smith I, Boyle F, Xu B, Gomez H, Suter T, Gelber RD, EA. J Clin Oncol. 2016 Apr 1;34(10):1034-42. doi: 10.1200/JCO.2015.62.1797. Epub 2015 Nov 23.

Other details about the study can be found in these articles:

- **Central Pathology Laboratory Review of HER2 and ER in Early Breast Cancer: An ALTTO Trial [BIG 2-06/NCCTG N063D (Alliance)] Ring Study.** McCullough AE, Dell'orto P, Reinholz MM, Gelber RD, Dueck AC, Russo L, Jenkins RB, Andrighetto S, Chen B, Jackisch C, Untch M, Perez EA, Piccart-Gebhart MJ, Viale G. Breast Cancer Res Treat. 2014 Feb;143(3):485-92. doi: 10.1007/s10549-013-2827-0. Epub 2014 Jan 7.
- **Lapatinib-Related Rash and Breast Cancer Outcome in the ALTTO Phase III Randomized Trial.** Sonnenblick A, de Azambuja E, Agbor-Tarh D, Bradbury I, Campbell C, Huang Y, Dueck AC, Pritchard KI, Wolff AC, Jackisch C, Lang I, Untch M, Smith I, Boyle F, Xu B, Gomez H, Perez EA, Piccart M, Azim HA Jr. J Natl Cancer Inst. 2016 Apr 20;108(8). pii: djw037. doi: 10.1093/jnci/djw037. Print 2016 Aug.

To learn about this trial, visit the ClinicalTrials.gov website at
https://clinicaltrials.gov/ct2/show/NCT00490139

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 April 2016.
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.