Alliance Public Study Result Summary
CALGB 40603

What this study is about

This study compared different drug treatments (chemotherapy) given before surgery for patients with triple-negative breast cancer, which is breast cancer without estrogen receptor (ER), progesterone receptor (PR) or HER2.

The full title of this study is: Randomized phase II 2 x 2 factorial trial of the addition of carboplatin +/- bevacizumab to neoadjuvant weekly paclitaxel followed by dose-dense AC in hormone receptor-poor/HER2-negative resectable breast cancer

Why the study was done

This study was done to see if adding either a chemotherapy drug called carboplatin (common brand name paraplatin) or a therapy that targets blood vessels called bevacizumab (common brand name avastin), increases the number of cancers that have disappeared at the time of surgery compared to a usual (standard) chemotherapy alone.

Researchers measured how many women who were diagnosed with triple-negative breast cancer had cancers that completely disappeared by the time of surgery. They also studied the safety of the treatments.

Study results

These results are for people with stage II or III triple-negative breast cancers. Patients whose cancers had very low levels of ER or PR (less than 10%) were also included.

The study found that adding either carboplatin or bevacizumab to a usual chemotherapy before surgery made breast cancer tumors go away in more patients by the time of surgery.

Adding carboplatin also got rid of more cancer in both the breast and in the lymph nodes under the arm. Bevacizumab did not do this.

Both carboplatin and bevacizumab increased the number of side effects and lowered the number of patients who were able to get all of the usual chemotherapy. Some of the side effects were serious.

The most common serious side effects with carboplatin included:

- Very low white blood cell levels. *This can cause infections.*
- Very low blood platelet levels. *This can cause excess bleeding.*

The most common serious side effects with bevacizumab included:

- High blood pressure
- Complications after surgery

Adding both carboplatin and bevacizumab together also increased levels of:

- Severe tiredness *(fatigue)*
- Fever with low white cells
- Severe pain

What the results mean

Adding carboplatin to usual chemotherapy that is given before surgery made more breast cancer tumors go away in both breast and underarm lymph nodes by the time of surgery. Carboplatin also increased the number of serious side effects.

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Adding bevacizumab to usual chemotherapy that is given before surgery made more cancer tumors go away in the breast but not in lymph nodes. Bevacizumab also increased the number of serious side effects.

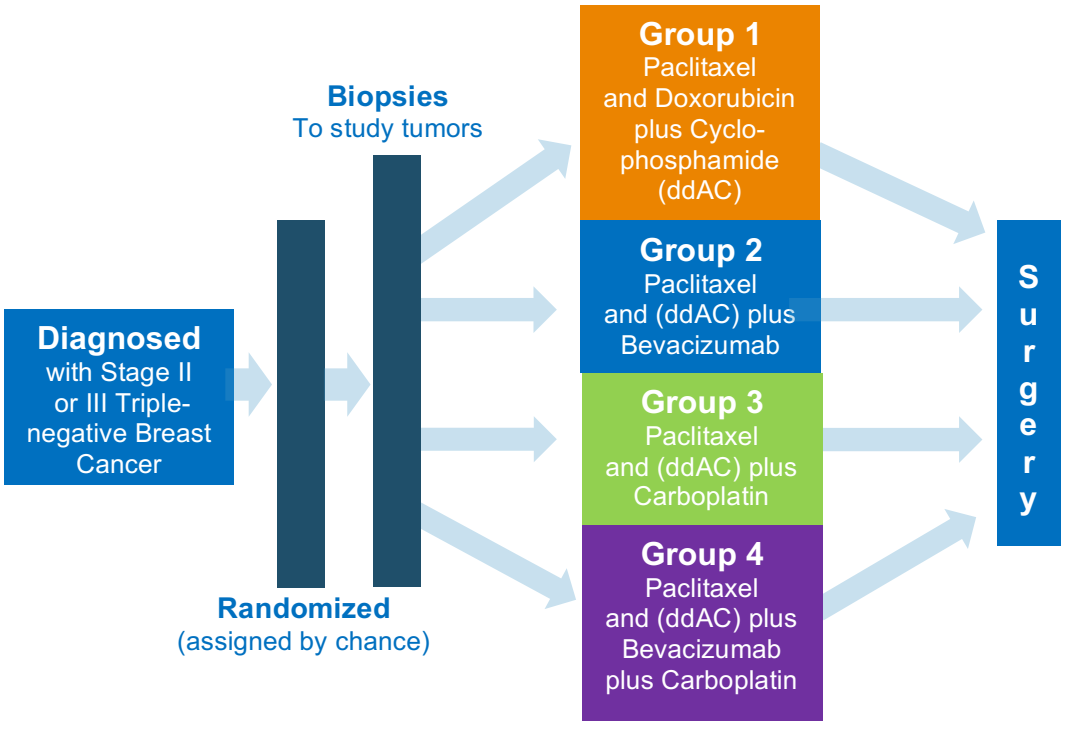
This study did not find out if patients who got carboplatin (or bevacizumab) are less likely to have their cancer return or if they will live longer. More study is needed before usual treatment would be changed.

How the study worked

All patients received the usual chemotherapy of paclitaxel (common brand name taxol) once a week for 12 treatments and then AC [the combination of doxorubicin (common brand name adriamycin) plus (common brand name cytoxan)] every two weeks for four treatments. Growth factor injections (common brands neupogen or neulasta) to help raise the white blood cell counts faster were used after each AC treatment.

Patients 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 usual chemotherapy, one quarter got just carboplatin, one quarter got just bevacizumab and one quarter got both.

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



When did the study start and end? The study started in May 2009. All patients were enrolled by August 2012. This study was done in the U.S. and Canada.

How many patients joined? 443 patients were treated 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:

- **Impact of the Addition of Carboplatin and/or Bevacizumab to Neoadjuvant Once-Per-Week Paclitaxel Followed by Dose-Dense Doxorubicin and Cyclophosphamide on Pathologic Complete Response Rates in Stage II to III Triple-Negative Breast Cancer: CALGB 40603 (Alliance).** Sikov WM, Berry DA, Perou CM, Singh B, Cirrincione CT, Tolaney SM, Kuzma CS, Pluard TJ, Somlo G, Port ER, Golshan M, Bellon JR, Collyar D, Hahn OM, Carey LA, Hudis CA, Winer EP. J Clin Oncol. 2015 Jan 1;33(1):13-21. doi: 10.1200/JCO.2014.57.0572. Epub 2014 Aug 4.

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

- **Impact of Neoadjuvant Chemotherapy in Stage II-III Triple Negative Breast Cancer on Eligibility for Breast-conserving Surgery and Breast Conservation Rates: Surgical Results from CALGB 40603 (Alliance).** Golshan M, Cirrincione CT, Sikov WM, Berry DA, Jasinski S, Weisberg TF, Somlo G, Hudis C, Winer E, Ollila DW; Alliance for Clinical Trials in Oncology. Ann Surg. 2015 Sep;262(3):434-9; discussion 438-9. doi: 10.1097/SLA.0000000000001417.
- **Axillary Management of Stage II/III Breast Cancer in Patients Treated with Neoadjuvant Systemic Therapy: Results of CALGB 40601 (HER2-Positive) and CALGB 40603 (Triple-Negative).** Ollila DW, Cirrincione CT, Berry DA, Carey LA, Sikov WM, Hudis CA, Winer EP, Golshan M. J Am Coll Surg. 2017 Apr;224(4):688-694. doi: 10.1016/j.jamcollsurg.2016.12.036. Epub 2017 Jan 13.

To learn about this trial, visit the ClinicalTrials.gov website at
https://clinicaltrials.gov/ct2/show/NCT00861705

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 January 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.