Alliance Public Study Result Summary

What this study is about

This study compared two different treatments for breast cancer patients who had no lymph nodes with cancer, or who had 1-3 lymph nodes with cancer. It also tested if 4 or 6 treatments worked better.

The full title of this study is: CALGB (Alliance) 40101 - Cyclophosphamide and doxorubicin (CA x 4 cycles) versus paclitaxel (4 cycles) as adjuvant therapy for breast cancer in women with 0-3 positive axillary lymph nodes: A phase III randomized study

Why the study was done

When this study began, doctors did not know the best way to treat patients with node negative (breast cancer only in the breast) or 1-3 node positive breast cancer. Both of these breast cancers are called low-risk primary breast cancer. Doctors wondered if they could give chemotherapy with less side effects, and fewer cycles of chemotherapy to patients with low-risk breast cancer.

This study tested how long chemotherapy should be given and if a single drug called paclitaxel (T) was as good as the common chemotherapy treatment that used two drugs called doxorubicin (A) and cyclophosphamide (C). This common treatment is known as AC.

Study results

These results are for patients with low-risk breast cancer that includes 0-3 positive lymph nodes.

The study found that:

- 4 cycles of chemotherapy was as good as 6 cycles of chemotherapy. There was no added gain from 2 more cycles.
- Patients who got 6 cycles of chemotherapy had more safety events.
- The single chemotherapy treatment with paclitaxel (T) was not as good as the common chemotherapy treatment with doxorubicin (A) and cyclophosphamide (C), but the differences were small.
- The AC treatment had more safety events than the T treatment.

Here are some of the most common safety events:

Safety events with the AC treatment included:

- More blood related problems like low blood counts with AC treatment. These events were more common with 6 cycles of AC.
- More heart related events for patients who got 6 cycles of AC treatment. This included 2 heart events shortly after getting AC that resulted in death for both patients.
- 7 of 1,931 patients treated with AC were diagnosed with leukemia.

Safety events with the T treatment included:

- More pain, numbness or tingling in their hands and feet (neuropathy) than those who got AC treatment.
- Fewer heart related events. No patients who got T died of heart related events.
- No patients who got T treatment had leukemia.

What the results mean

AC remains a common treatment for breast cancer patients with no lymph nodes involved with cancer, or 1-3 positive lymph nodes involved (low-risk breast cancer). Patients treated with T were more likely to have their cancer return, but the differences were small. Four cycles of chemotherapy is as good as 6 cycles, so women can be spared 2 extra cycles that can add more safety events. Patients treated with AC were more likely to have heart safety events or to develop leukemia, though

both were rare. Patients treated with T were more likely to have weakness, numbness and pain from nerve damage, often in the hands and feet.

How the study worked

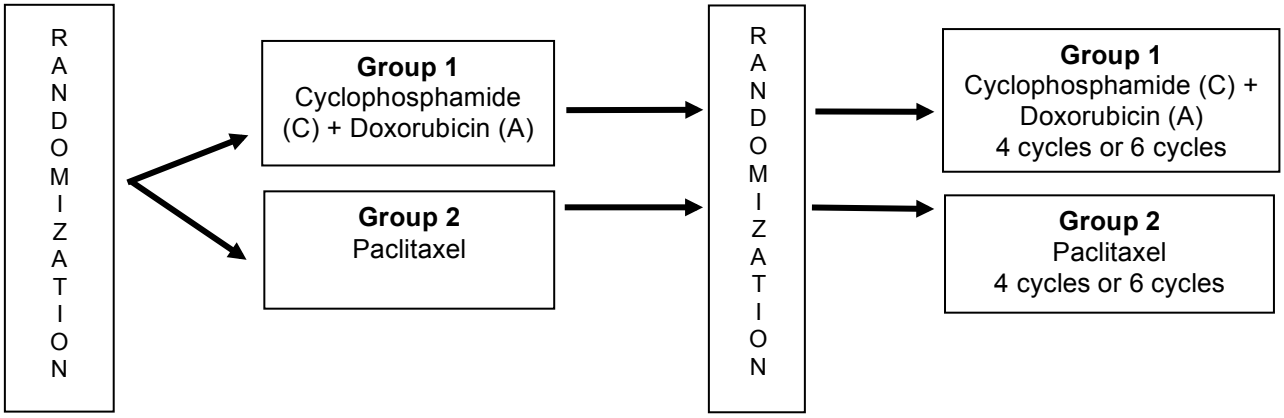
Low-risk breast cancer includes patients who have no lymph nodes that have cancer, and patients who have 1-3 lymph nodes that have cancer cells (called lymph node positive).

Patients were put into 2 groups by chance (randomized) to reduce differences between the groups. This was done because no one knew if one treatment was better than another.

- **Group A**: Half of the patients got a combined therapy of two drugs that is commonly given. The combined treatment includes doxorubicin (A) and cyclophosphamide (C), and is called AC treatment.
- **Group B**: The other half got one drug called paclitaxel *(*Taxol®) by itself.

After the groups were chosen, they were randomized again to get 4 cycles or 6 cycles of their treatment. Patients were followed for safety events, to see if their cancer came back over time (a recurrence), and how long they lived (overall survival).

Here is a picture that explains how patients were placed into one of 2 groups.



When did the study start and end? The study started in 2002. All patients were enrolled by 2010

How many patients joined? 3,871 patients agreed to be in this study

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

Scientific publications about this study

Details about the study can be found in these articles:

- Comparison of Doxorubicin and Cyclophosphamide Versus Single-Agent Paclitaxel As Adjuvant Therapy for Breast Cancer in Women With 0 to 3 Positive Axillary Nodes: CALGB 40101 (Alliance)
  Shulman LN, Berry DA, Cirrincione CT, et al. *Journal of Clinical Oncology, 1;32(22):2311-7,2014. doi: 10.1200/JCO.2013.53.7142. Epub 2014 Jun 16.*
- Polygenic Inheritance of Paclitaxel-Induced Sensory Peripheral Neuropathy Driven by Axon Outgrowth Gene Sets in CALGB 40101 (Alliance)
  Chhibber A, Mefford J, Stahl EA, et al. *Pharmacogenomics Journal, 14(4):336-42, 2014. doi: 10.1038/tpj.2014.2. Epub 2014 Feb 11.*

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To learn about this trial, visit the ClinicalTrials.gov website at – https://clinicaltrials.gov/show/NCT00041119.

This study was sponsored by the Cancer and Leukemia Group B (CALGB) which is part of the Alliance for Clinical Trials in Oncology – a national cooperative network 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 February 2015. New Information may be available.

We thank the people who joined this study and made it possible. *This study could have been completed faster if more people who had the opportunity to participate would have done so. If you know people who are offered the chance to join a cancer clinical trial, please encourage them to enroll. 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. We appreciate your advocating for federally-funded research to your elected representatives.