Alliance Public Study Result Summary
CALGB 10603

What this study is about

A study that compared different chemotherapy treatment drugs in patients with leukemia cells with the abnormal FLT3 gene.

The full title of this study is: A phase III randomized, double-blind study of induction (daunorubicin/cytarabine) and consolidation (high-dose cytarabine) chemotherapy + midostaurin (PKC412) (IND #101261) or placebo in newly diagnosed patients < 60 years of age with FLT3 mutated acute myeloid leukemia (AML)

Why the study was done

This study was done to see if adding a new drug to standard chemotherapy was as good or better than chemotherapy alone for patients aged 18 to 59 years old with acute myeloid leukemia (AML) with the FLT3 gene mutation.

Half the patients got a new drug called midostaurin (common brand name Rydapt) with chemotherapy. Midostaurin was given as a pill, and the chemotherapy was given through the vein (IV). The other half of the patients got only chemotherapy, which is the most common treatment for AML. This chemotherapy for both groups included 7+3: cytarabine (common brand name Cytosar) given by IV for 7 days continuously and daunorubicin (common brand name cerubidine) given by IV once daily for 3 days.

These treatments were given in a hospital and required that patients stay in the hospital for several weeks.

The study was done to see how well the treatments worked. The study wanted to learn if patients would live longer by adding midostaurin to chemotherapy than if they only received chemotherapy by itself.

Study results

These results are for younger adults between the ages of 18-59 years old with newly diagnosed AML with the FLT3 mutation.

The study found that:

- About half (55-60 out of 100) of patients treated in both groups had their leukemia go away (complete remission)
- Patients treated with midostaurin and chemotherapy lived longer than patients that received chemotherapy alone.
- Patients treated with midostaurin and chemotherapy had more time before their leukemia came back than patients that received chemotherapy alone.
- Patients treated in both groups had similar side effects and the addition of midostaurin to chemotherapy did not make patients feel sicker.

The most common serious side effects included:

- Low white blood cells, low red blood cells (anemia), and low platelets.
- Fever due to low white blood cells called neutrophils (help fight infections) was seen in 80 of 100 patients
- Infection due to low white blood cell counts was seen in 50 of 100 patients.

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What the results mean

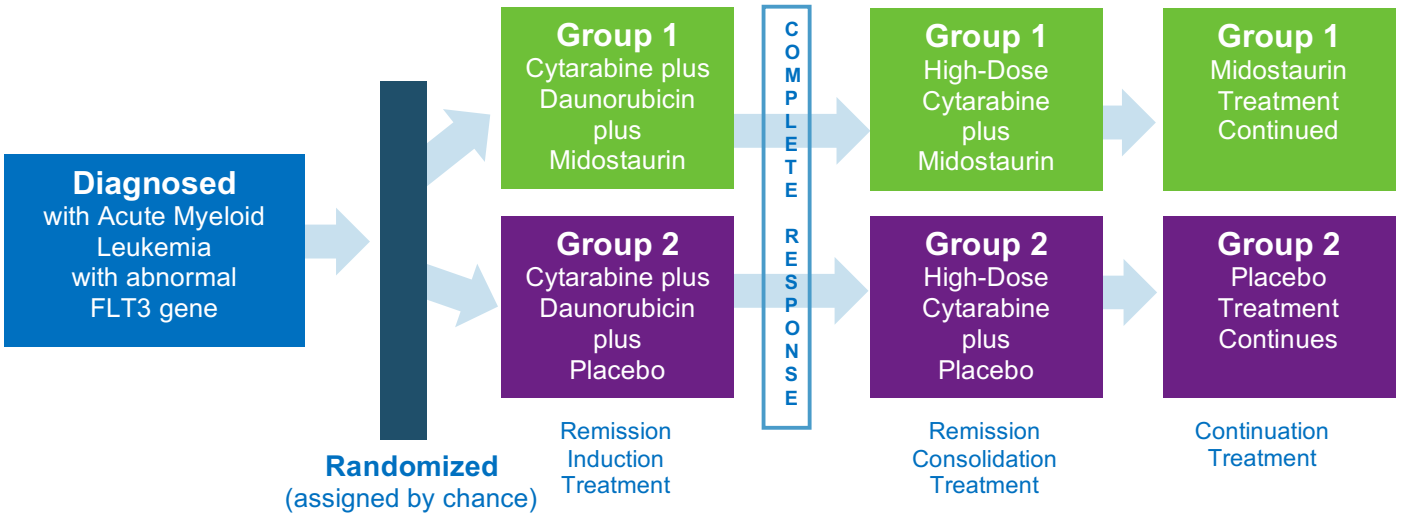
This means that midostaurin and chemotherapy work better for patients with AML with the FLT3 mutation than chemotherapy by itself.

These results are for younger adults between the ages of 18-59 years old who have new AML with the FLT3 mutation that has not yet been treated.

How the study worked

Patients were assigned by chance (randomized) to one of two groups. This made sure that each patient had the same chance of being in any study group. One of the two groups got the usual treatment with a pill that had no medicine - *this is called a placebo pill.*

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



Patients received induction treatment with either:

- 7+3 followed by placebo on days 8-21

OR

- 7+3 followed by midostaurin on days 8-21

If patients did not have leukemia in the bone marrow (complete remission) after induction treatment they received 4 cycles (each a total of 28 days) of consolidation treatment with either:

- High dose cytarabine on days 1, 3, 5 followed by placebo on days 8-21

OR

- High dose cytarabine on days 1, 3, 5 followed by midostaurin on days 8-21

Patients were not required to have a stem cell transplant as part of the study. Patients made the decision to have a stem cell transplant based on discussions with their doctors.

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

How many patients joined? 717 patients agreed to be in 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:

- **Midostaurin plus Chemotherapy for Acute Myeloid Leukemia with a FLT3 Mutation.** Stone R, Mandrekar S, Sanford B, Laumann K, Geyer S, Bloomfield C, Thiede C, Prior T, Döhner K, Marcucci G, Lo-Coco F, Klisovic R, Wei A, Sierra J, Sanz M, Brandwein J, Witte Td, Niederwieser D, Appelbaum F, Medeiros B, Tallman M, Krauter J, Schlenk R, Ganser A, Serve H, Ehninger G, Amadori S, Larson R, Döhner H. N Engl J Med. 2017 Jun 23. doi: 10.1056/NEJMoa1614359. [Epub ahead of print]

Other details about the study can be found in this article:

- **CALGB 10603 (RATIFY): A Randomized Phase III Study of Induction (Daunorubicin/Cytarabine) and Consolidation (High-Dose Cytarabine) Chemotherapy Combined With Midostaurin Or Placebo in Treatment-naive Patients with FLT3 Mutated AML.** Stone RM, Dohner H, Ehninger G, et al. [Abstract] J Clin Oncol 29 (Suppl 15): A-TPS199, 2011.

To learn about this trial, visit the ClinicalTrials.gov website at
https://clinicaltrials.gov/ct2/show/NCT00651261

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 June 2017.
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.