Title

CALGB 9702—Phase III study of MDR modulation with PSC-833 (NSC # 648265) followed by immunotherapy with rIL-2 (NSC # 373364) vs no further therapy in previously untreated patients with AML ≥ 60 years

Simple tile: CALGB 9720: A study in acute myeloid leukemia (AML) that compared different ways to give treatment to patients who were 60 years and older

Why the study was done

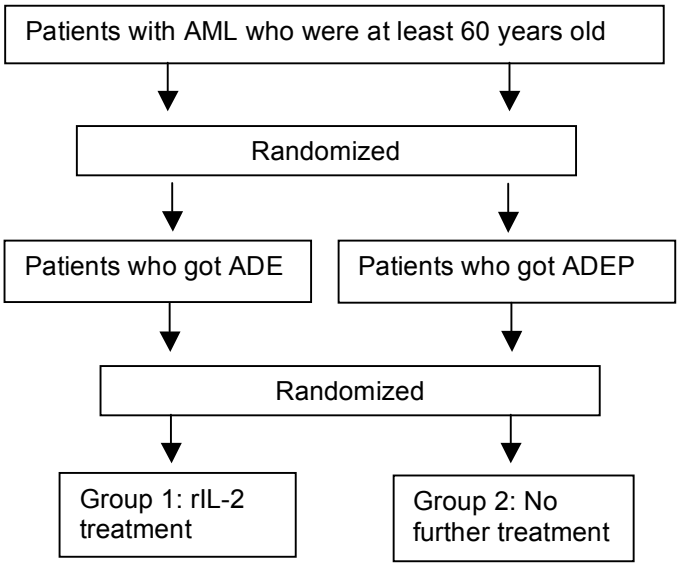
This study was done in two parts.

Part 1: MDR (or multidrug resistance) happens when cancer cells create a protein that pumps drugs (chemotherapy) out of the cells. Research has shown that certain drugs can block these pumps so that chemotherapy drugs can get into the cancer cells. The first part of this study was done to see if a new drug called PSC-833 could improve response to chemotherapy by blocking the pump in cancer cells. This study was for newly diagnosed acute myeloid leukemia (AML) patients who were 60 years and older at the time of treatment. To do this, the standard treatment of cytarabine (Cytosar®), daunorubicin (Cerubidine®) and etoposide (Vepesid®) (called "ADE)" was compared to the same treatment with PSC-833 (called "ADEP").

Part 2: Some cancer cells are killed when they come into contact with cells called "killer" cells that are in the body's immune system. Drugs called cytokines that include interleukin-2 (IL-2) can make this happen. The second part of this study was done to see if taking IL-2 after treatments in Part 1 led to more time before AML came back, or kept it from coming back at all.

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

Here is a picture that explains how patients were placed into groups:



When did the study start and end? The study started in March 1998. All patients were enrolled by May 2002.

How many patients participated?

A total of 669 patients were in the study. 120 patients agreed to be in Part 1 of this study, and 61 got ADE while 59 got ADEP. 163 patients who finished chemotherapy agreed to be in Part 2 of this study. Most of them received ADE in Part 1 because researchers stopped using ADEP treatment.

Study results

Important findings:

- The same number of patients (33 out of 100) lived one year after being diagnosed with AML, whether they got ADE or ADEP treatment. This study confirmed earlier studies that showed how serious AML is in patients 60 years old and older.
- Patients who got the ADE treatment had less jaundice (yellow skin) and fewer problems with their liver (one in four patients with ADE compared to one in two patients with ADEP). Researchers stopped giving the ADEP treatment once this was learned.
- There was no difference between IL-2 or no further treatment. Patients lived without disease for the same amount of time, no matter which group they were in.

Other important findings: Leukemia cells from this study helped find out more about how patients will do when they have normal chromosomes (DNA and protein) in their leukemia cells. People who have changes in different genes, such as NPM1, FLT3 and others respond better or worse to treatment for AML. More studies are needed before doctors can base treatments on these results.

What the results mean

Adding PSC-833 to block a protein that pumps chemotherapy drugs out of cancer cells did not help patients live longer, and the drug gave patients more liver problems. The study also found that adding IL-2 after chemotherapy did not help people live longer.

These results are for people who are 60 years and older and have AML.

Scientific publications about this study

Details about the study can be found in these articles:

- *FLT3* internal tandem duplication associates with adverse outcome and gene- and microRNA-expression signatures in patients 60 years of age or older with primary cytogenetically normal acute myeloid leukemia: A Cancer and Leukemia Group B study
  Whitman SP, Maharry K, Radmacher MD, Becker H, Mrózek K, Margeson D, Holland KB, Wu Y-Z, Schwind S, Metzeler KH, Wen J, Baer MR, Powell BL, Carter TH, Kolitz JE, Wetzler M, Moore JO, Stone RM, Carroll AJ, Larson RA, Caligiuri MA, Marcucci G, Bloomfield CD
  Blood 116:3622, 2010
- Prognostic impact of Wilms tumor 1 gene (WT1) mutations in older de novo cytogenetically normal acute myeloid leukemia (CN-AML): A Cancer and Leukemia Group B study
  Becker H, Marcucci G, Maharry K, Radmacher MD, Mrózek K, Margeson D, Whitman SP, Paschka P, Holland KB, Schwind S, Wu Y-Z, Powell BL, Carter TH, Kolitz JE, Wetzler M, Carroll AJ, Baer MR, Caligiuri MA, Larson RA, Bloomfield CD.
  Blood 116:788-792, 2010
- Favorable prognostic impact of NPM1 mutations in older patients with cytogenetically normal de novo acute myeloid leukemia and associated gene- and microRNA-expression signatures: A Cancer and Leukemia Group B study
  Becker H, Marcucci G, Maharry K, Radmacher MD, Mrózek K, Margeson D, Whitman SP, Wu YZ, Schwind S, Paschka P, Powell BL, Carter TH, Kolitz JE, Wetzler M, Carroll AJ, Baer MR, Caligiuri MA, Larson RA, Bloomfield CD
  Journal of Clinical Oncology 28 (4) 596-604, 2010
- Low-dose interleukin-2 immunotherapy does not improve outcome of patients age 60 years and older with acute myeloid leukemia in first complete remission: Cancer and Leukemia Group B study 9720
  Baer MR, George SL, Caligiuri MA, Sanford BL, Bothun SM, Mrózek K, Kolitz JE, Powell BL, Moore JO, Stone RM, Anastasi J, Bloomfield CD, Larson RA

Journal of Clinical Oncology 26 (25):4934-4939, 2008

- Cancer and Leukemia Group B studies of recombinant interleukin-2 maintenance therapy in acute myeloid leukemia
  Baer MR, Kolitz JE, George SL, Caligiuri MA, Larson RA.
  Annals of Hematology 87(Supplement 1):S28-S30, 2008
- Pretreatment cytogenetics add to other prognostic factors predicting complete remission and long-term outcome in patients 60 years of age or older with acute myeloid leukemia: Results from Cancer and Leukemia Group B 8461
  Farag SS, Archer KJ, Mrózek K, Ruppert AS, Carroll AJ, Vardiman JW, Pettenati MJ, Baer MR, Qumsiyeh MB, Koduru PR, Ning Y, Mayer RJ, Stone RM, Larson RA, Bloomfield CD
  Blood 108(1):63-73, 2006
- Cancer and Leukemia Group B (CALGB) multidrug resistance modulation trials in untreated acute myeloid leukemia
  Kolitz JE, George SL, Baer MR, Lee EJ, Bloomfield CD, Larson RA
  Annals of Hematology 85(Supplement 1):78-79, 2006
- Differences in prognostic factors and outcomes in African Americans and whites with acute myeloid leukemia
  Sekeres MA, Peterson B, Dodge RK, Mayer RJ, Moore JO, Lee EJ, Kolitz J, Baer MR, Schiffer CA, Carroll AJ, Vardiman JW, Davey FR, Bloomfield CD, Larson RA, Stone RM for the Cancer and Leukemia Group B (CALGB)
  Blood 103(11):4036-4042, 2004
- Adult de novo acute myeloid leukemia with t(6;11)(q27;q23): Results from Cancer and Leukemia Group B study 8461
  Blum W, Mrózek K, Ruppert AS, Carroll AJ, Rao KW, Pettenati MJ, Anastasi J, Larson RA, Bloomfield CD
  Cancer 101(6):1420-1427, 2004
- Is modulation of multidrug resistance a viable strategy for acute myeloid leukemia?
  Larson RA
  Leukemia 17(3):488-491, 2003
- Phase 3 study of the multidrug resistance modulator PSC-833 in previously untreated patients 60 years of age and older with acute myeloid leukemia: Cancer and Leukemia Group B Study 9720
  Baer MR, George SL, Dodge RK, O'Loughlin KL, Minderman H, Caligiuri MA , Anastasi J , Powell BL, Kolitz JE , Schiffer CA, Bloomfield CD, Larson RA
  Blood 100(4):1224-1232, 2002

You can also talk with your doctor for more information.

This sheet reviews what is known about this research study as of March 2011. New Information may be available.

This study was sponsored by the Cancer and Leukemia Group B (CALGB) – a national cooperative group that conducts large-scale cancer clinical trials. The CALGB is supported by the National Cancer Institute (NCI) and brings together scientists to develop better treatments for cancer.

Research studies (or clinical trials) are done to learn what treatments work better in people than what we already have. Thank you for your interest in learning more about cancer research advances.