This is a summary of a clinical study in older patients with cancer. It is written for the general reader and uses language that is easy to understand. It includes information about how researchers did the study and what the results were. The simplified title for the study is: 'A study of volasertib and cytarabine compared with cytarabine alone in older patients with acute myeloid leukaemia'.

We thank all patients who took part in this study. Through your participation, you helped researchers answer important questions about volasertib and the treatment of cancer.

What was this study about?

Older patients (aged 65 years or older) with acute myeloid leukaemia (AML) took part in this study. The purpose of this study was to test whether adding the medicine volasertib to the standard chemotherapy treatment with cytarabine helps patients with AML. During the study, researchers also collected information on unwanted effects of volasertib and cytarabine.

This study started in February 2013. Some patients are still in the study, but the final analysis shown in this summary was done in June 2017. The sponsor of this study is Boehringer Ingelheim.

Why was the study needed?

New treatments for AML are needed. AML is a fast growing cancer in the blood and the bone marrow. The bone marrow is the spongy part of bone where blood cells are made. AML causes abnormal blood cells to build up so the body can no longer fight infections or stop bleeding. AML is diagnosed most often in patients older than 65 years of age. Very few of these patients survive 5 years after the diagnosis. Younger adult patients have treatment options like intensive chemotherapy or bone marrow transplantation. However, older patients are usually not strong enough to tolerate such therapies. Cytarabine is the current standard treatment for these older patients, but it is not likely to cure AML.

Which medicines were studied?

- Volasertib (BI 6727) is a new medicine, which is given by infusion into a vein. It works by blocking the ability of cancer cells to grow and spread throughout the body.
- Cytarabine is a chemotherapy that is routinely used to treat patients with AML. It is given as an injection under the skin. Cytarabine also works by blocking the ability of cancer cells to grow and spread, but it works in a different way.

Who participated in the study?

Patients with AML who were 65 years old or older participated in this study. They had not yet received any treatment for their AML before entering this study. They could not receive intensive treatments for AML because of their advanced age or because they had other serious health problems.

Overall, 661 patients were treated in the study. The average age was 75 years. The youngest patient was 65 years old and the oldest patient was 93 years old.

The table below shows the number of patients in different geographical regions and countries who were treated in the study.

Geographical Region	Countries	Number of Patients
Western Europe	Austria, Belgium, Finland, France, Germany, Greece, Italy, Netherlands, Norway, Portugal, Spain	441 patients
East Asia	Japan, Korea, Taiwan	107 patients
Other countries	Argentina, Brazil, Canada, Czech Republic, Hungary, India, Mexico, Poland, Russia, South Africa, United States	113 patients

How was this study done?

At the beginning of the study, 440 patients received volasertib and cytarabine, and 221 patients received cytarabine only. It was decided by chance who got which treatment. Patients in the cytarabine group also received a placebo. Placebo was a liquid that looked like volasertib but contained no medicine. In this way, neither patients nor doctors knew whether the patients were taking volasertib with the cytarabine.

Patients who were taking volasertib started on a dose of 350 milligrams (mg). Volasertib or placebo was given on the first day and then on the fifteenth day of each treatment cycle. A treatment cycle lasted 28 days. The dose of volasertib could be decreased if the patients had unwanted effects that they could not tolerate. All patients also took a low dose (20 mg) of cytarabine twice a day during the first 10 days of each treatment cycle.

After about 1 year and 9 months of the study, the first planned analysis was done. This analysis showed safety concerns and no improvement in patients' survival with the volasertib and cytarabine treatment. For this reason, all patients and their doctors were made aware of the treatment the patients had been receiving. They were given the choice to continue treatment with volasertib and cytarabine, or with cytarabine alone, or to stop all treatment in the study.

Patients could receive the study medicines until their AML got worse, or until the patient had an unwanted effect they could not tolerate.

All patients followed the same general procedures repeated for each 28-day treatment cycle:

- Patients visited the study doctor regularly each week.
- At these visits, blood was collected for safety tests.
- At some visits, the cells in bone marrow were checked for disease.
- At all visits, the doctors collected information on unwanted effects.

The doctors looked after each patient and checked their results. The doctors did more medical tests when needed.

Researchers wanted to see if volasertib with cytarabine could lead to remission of AML. Remission meant there were no or only a few cancer cells remaining in the bone marrow and in the blood. This is called an 'objective response'. They also wanted to see if there was an increase in the amount of time before the patient died from AML or from any other cause. This is called 'overall survival'.

What were the results of this study?

After about 4 years and 3 months of the study, the final analysis was done. About 28% of patients in the volasertib with cytarabine treatment group and 17% of patients in the cytarabine treatment group had remission of their AML.

The average overall survival time was 5.6 months for the volasertib with cytarabine treatment group and 6.5 months for the cytarabine treatment group. The risk of dying was about the same for patients taking volasertib with cytarabine and for patients taking cytarabine only. At the time of the final analysis, about 85% of patients in the volasertib with cytarabine treatment group had died. About 90% of patients in the cytarabine treatment group had died.

No clear conclusions could be made because the study had been changed before the time of the final analysis. The change was that both doctors and patients found out about which treatment patients were receiving.

What unwanted effects did patients have?

Most patients had at least 1 unwanted effect. There were 80% of patients taking volasertib and cytarabine and 73% of patients taking cytarabine who had unwanted effects.

The table below shows the most common unwanted effects that at least 20% of patients in either group had.

Doctors keep track of all health problems patients have during a study. Some of these health problems might be caused by the study medicines, and some by other medicines taken by the patient. Others might be caused by the disease, and some have yet a different cause. Here we describe health problems that the doctors thought were caused by the study medicines. These health problems are called unwanted effects.

	Volasertib and cytarabine (439 patients)	**Cytarabine (222 patients)**
Patients with any unwanted effect	352 patients (80%)	163 patients (73%)
Fever with a reduced number of a type of white blood cells (febrile neutropenia)	165 patients (38%)	43 patients (19%)
Reduced number of blood platelets (thrombocytopenia)	152 patients (35%)	58 patients (26%)
Reduced number of red blood cells (anaemia)	127 patients (29%)	47 patients (21%)
Reduced number of a type of white blood cells (neutropenia)	117 patients (27%)	31 patients (14%)
Nausea	58 patients (13%)	52 patients (23%)

Some patients in the study had serious unwanted effects. An unwanted effect was serious if it caused the patient to go to the hospital or stay longer in the hospital. It was also serious if it needed a doctor's immediate attention, was life-threatening, or caused death.

A total of 223 out of 439 patients (51%) in the volasertib and cytarabine group and 70 out of 222 patients (32%) in the cytarabine group had a serious unwanted effect. The most common serious unwanted effects for both groups were fever with a reduced number of a type of white blood cells (febrile neutropenia) and lung infection (pneumonia).

There were 34 patients out of 439 patients (8%) in the volasertib and cytarabine group and 11 patients out of 222 patients (5%) in the cytarabine group who died due to unwanted effects that the doctor thought could have been caused by the study medicine.

Are there follow-up studies?

No follow-up studies are planned.

Where can I find more information?

You can find the scientific summaries of the study results at these websites:

www.trials.boehringer-ingelheim.com	search for the study number: 1230.14
www.clinicaltrialsregister.eu	search for the EudraCT number: 2012-002487-27
www.clinicaltrials.gov	search for the NCT number: NCT 01721876

The full title of the study is:

'A Phase III randomised, double-blind, controlled, parallel group study of intravenous volasertib in combination with subcutaneous low-dose cytarabine vs. placebo + low-dose cytarabine in patients ⩾65 years with previously untreated acute myeloid leukaemia, who are ineligible for intensive remission induction therapy'.

Important notice

This summary shows only the results from one study and may not represent all of the knowledge about the medicine studied. Usually, more than one study is carried out in order to find out how well a medicine works and the side effects of the medicine. Other studies may have different results.

You should not change your therapy based on the results of this study without first talking to your treating physician. Always consult your treating physician about your specific therapy.

Boehringer Ingelheim has provided this lay summary in accordance with European Union transparency obligations.