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 in patients with acute myeloid leukaemia to find the highest dose of volasertib that patients could bear when given with decitabine'.

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. Researchers wanted to find the highest dose of volasertib that patients could take when given with decitabine without having certain side effects. To achieve this, they collected information on the side effects of volasertib when taken with decitabine.

This study started in February 2014 and finished in May 2016. This study was stopped early because the sponsor decided not to further develop volasertib. The sponsor of this study was Boehringer Ingelheim.

Why was the study needed?

AML is a fast-growing cancer in the blood and the bone marrow, which is the spongy part of bone where blood cells are made. It 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, and very few of these patients survive 5 years after the diagnosis. Young adult patients have treatment options like intensive chemotherapy or bone marrow transplantation. These therapies have been used to successfully treat AML in young patients. However, older patients are often more difficult to treat because they are not as strong and can have additional health issues. Also, the available therapies for older patients are not as likely to cure AML.

Which medicines were studied?

Every patient in the study took 2 medicines:

- Volasertib (also called 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.
- Decitabine is a medicine that is routinely used to treat older patients with AML. It is also given by infusion into a vein and works by blocking the ability of cancer cells to grow and spread. In the previous studies, it seemed to help older patients with AML to reduce their disease.

Who participated in the study?

Patients with AML who were 65 years old or older participated in this study. Most patients (10 out of 13) had received other chemotherapy in the past for AML. They had no other serious health problem that would preclude their treatment with decitabine. However, most patients did have some health problems due to their age and due to certain medicines that they had already received.

The study planned for at least 127 patients in the United States to take part. However, because the study was stopped early, only 13 patients took part. There were 7 men and 6 women who took the study medicines. The average age was 73 years. The youngest patient was 66 years old and the oldest patient was 84 years old.

How was this study done?

All patients took volasertib in combination with decitabine on a regular schedule. Researchers wanted to know the highest dose of volasertib with decitabine that patients could tolerate. To find this dose, doctors gave increasing doses of volasertib to different small groups of patients. The first group of patients to enter the study started taking 300 milligrams (mg) of volasertib. The next group of patients was given 350 mg, and the next group was given 400 mg.

The study doctors checked each group for certain severe side effects. They determined the dose at which no more than 1 out of 6 patients had such side effects. This dose was the maximum tolerated dose. It was determined in the first treatment cycle, which took 4 weeks in this study.

There were 4 parts of the study planned. Each part was to test a different schedule of the volasertib and decitabine combination. However, since the study was stopped early, patients only participated in the first part (Schedule A).

A patient was treated in several treatment cycles as long as the conditions to stop treatment were not reached. Each treatment cycle also included a period of rest.

Both the study doctor and the patients knew what dose of study medicines the patients were getting. The dose of decitabine was based on the patient's body size (20 mg per square metre of body surface area, or m^2). Decitabine was given for the first 5 days of every treatment cycle. Volasertib was given on the first day and then on the 15^{th} day of every treatment cycle.

Patients were to receive the study medicines until their cancer symptoms got worse, or until the patients had side effects they could not tolerate.

All patients followed the same general procedures repeated for each 4-week treatment cycle:

- Patients visited the study doctor regularly each week.
- At these visits, blood was collected for safety tests, and patients answered questions about their health. Heart rhythm was measured at the visits when the patient received an infusion of either of the study medicines.
- At some visits, the cells in bone marrow were checked for disease.
- At all visits, the doctors collected information on side effects.

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

What were the results of this study?

It was determined that 400 mg of volasertib was the maximum tolerated dose when taken with 20 mg/m^2 of decitabine. This was the highest planned dose for the study. Because the study was stopped early, results were available for only 1 out of 4 planned parts of the study.

What side effects did patients have?

Most patients in this study (9 patients out of 13 patients, or 69%) had side effects. Seven patients (54%) had at least 1 severe side effect.

The table below shows severe side effects that occurred in at least 2 patients.

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 side effects.

	Volasertib and Decitabine 13 patients
Patients with any severe side effect	7 patients (54%)
Fever with a low level of a type of white blood cells (febrile neutropenia)	2 patients (15%)
Low level of red blood cells (anaemia)	2 patients (15%)
Lower level of a type of white blood cells (neutrophil count decreased)	2 patients (15%)

Some patients in the study had serious side effects. A side 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.

Overall, 6 of 13 patients (46%) had at least 1 serious side effect. The serious side effects that were reported by 2 patients each were:

- Fever with a low level of a type of white blood cells (febrile neutropenia)
- Low level of all types of blood cells (pancytopenia)

All other serious side effects were reported by single patients.

Four patients died while in the study. One of these patients in the 400 mg group died due to a low level of red blood cells (anaemia) that study doctors thought was related to the study medicine. The study doctors thought that the other 3 deaths were not related to 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: 1230.30
www.clinicaltrials.gov	search for the NCT number: NCT02003573

The full title of the study is:

'An open label, Phase I, dose escalation trial to investigate the maximum tolerated dose, safety, pharmacokinetics, and efficacy of volasertib in combination with decitabine in patients ≥65 years with acute myeloid leukemia'.

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 done to find out how well a medicine works and the side effects of the medicine. Other studies may have different results.

You should consult the prescribing information for your country to get more information on the medicine studied, or ask your physician about the medicine. You should not change your therapy based on the results of this study without first talking to your physician. Always consult your physician about your specific therapy.

Boehringer Ingelheim has provided this lay summary in accordance with transparency obligations. This lay summary is intended for audiences located within the European Union.