This is a summary of a clinical study of a medicine called idarucizumab in patients who take another medicine called dabigatran. 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 to test how well idarucizumab stops the anti-blood-clotting effect of dabigatran. Patients were in an emergency situation where bleeding had to be controlled'.

We thank all patients who took part in this study. Through your participation, you helped researchers answer important questions about idarucizumab and its effect on dabigatran.

This study started in June 2014 and finished in October 2016. The sponsor of this study was Boehringer Ingelheim.

Why was the study needed?

The purpose of the study was to examine how well idarucizumab restores normal blood clotting in patients taking dabigatran.

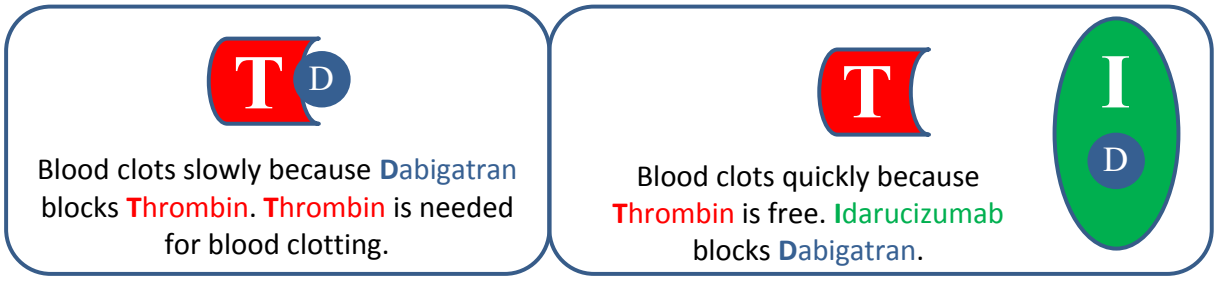
Anti-blood-clotting medicines like dabigatran are often taken by people with heart rhythm problems. Conditions such as these may cause a blood clot to form in the heart. If such a blood clot is transported to the brain, it can cause a stroke. Blood clots can also lead to a deep vein thrombosis, which is a blood clot, usually in a leg, which may cause pain, swelling, or redness. Dabigatran prevents the blood from clotting in these situations. Dabigatran therefore lowers the risk that these medical conditions occur or recur.

Patients may sometimes have accidents, or rarely, unexpected bleeding events. Accidents may need to be treated with emergency surgery. Bleeding during surgery needs to be minimized. Like any other blood thinner, dabigatran affects blood clotting. Normal blood clotting must be restored quickly before the doctor can begin surgery or other treatment. Idarucizumab is given to stop the effects of dabigatran, allowing the doctor to begin treatment for the emergency immediately.

The study doctors also collected information on side effects.

Which medicine was studied?

The medicine studied was idarucizumab (BI 655075). Idarucizumab is a medicine that stops the effects of a medicine called dabigatran. Dabigatran is a medicine that helps to prevent blood from clotting. The figure on the next page shows how idarucizumab stops the effects of dabigatran.



Who participated in the study?

Most patients had heart rhythm problems, and all patients were taking dabigatran. Patients must have had a medical emergency to be in the study, such as a car accident, a fall, or uncontrolled bleeding.

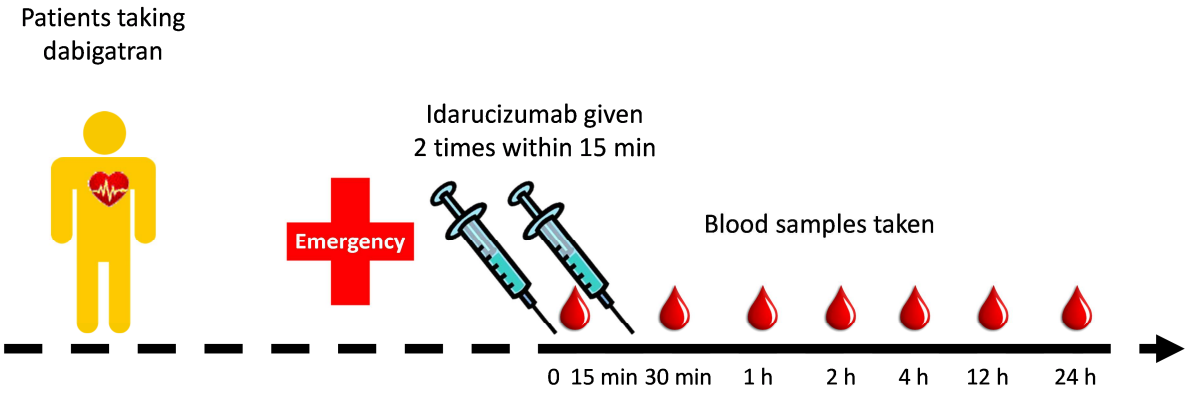
Patients were entered into the study because they had either uncontrolled bleeding or other emergencies that required immediate attention. This study tested whether idarucizumab could stop the effects of dabigatran in these patients.

A total of 503 patients were treated in this study. Almost all patients were elderly. Some had serious illnesses such as high blood pressure, heart failure, diabetes, a prior stroke, bleeding, or cancer. Other patients had serious injuries due to a bad accident. The average age was 77 years. The youngest patient was 21 years old and the oldest patient was 96 years old. There were 274 men (55% of patients) and 229 women (46%). Patients were from:

- Europe (225 patients)
- Australia-New Zealand (156 patients)
- North America (64 patients)
- Asia (31 patients)
- Latin America (6 patients)
- 4 other countries (21 patients)

How was this study done?

In this study, patients were treated in a real-world emergency situation. Either the patients were bleeding or they needed emergency surgery for a condition unrelated to dabigatran. They received idarucizumab intravenously. This means that the medicine was given directly in a vein in the arm. Patients with uncontrolled bleeding who needed medical help were entered into Group A. Patients who needed emergency surgery were entered into Group B. The patients and the study doctors knew that both groups were being treated with idarucizumab. Each patient received idarucizumab only on the day of the emergency. Patients received 1 dose of idarucizumab given in 2 shots. The shots were given within a maximum of 15 minutes of each other. The total dose was 5 g. In addition, patients received all other treatments their doctor thought were necessary due to their emergency. The 5 days after getting idarucizumab were called the ‘on-treatment period’. The figure on the next page shows how the study was conducted.



Researchers wanted to know if blood clotting returned to normal after idarucizumab was given. 'Normal' meant that blood would clot as quickly as in a person who did not take dabigatran. Researchers call this the reversal effect of idarucizumab. Researchers analysed the average (median) maximum reversal.

The procedures during the emergency surgeries and treatments varied from patient to patient. However, the following procedures were completed for patients in the study where possible:

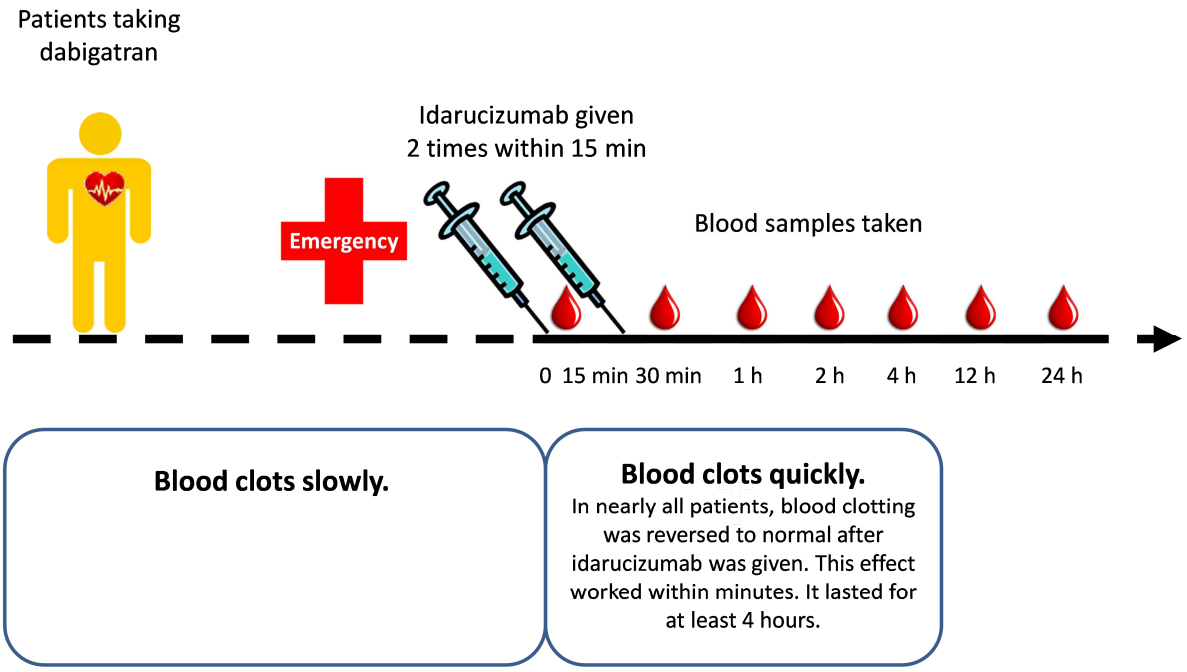
- Study doctors collected blood samples at 6 time points within the first 24 hours after a patient took idarucizumab.
- Study doctors checked patients for any side effects.

Researchers measured the time it took for a patient's blood samples to clot before and after the patient got idarucizumab. These blood-clotting times helped researchers to learn about the ability of idarucizumab to block the effects of dabigatran.

What were the results of this study?

In nearly all patients, blood clotting was reversed to normal condition after idarucizumab was given. This effect happened quickly within a few minutes after idarucizumab was given. For the majority of patients the effect lasted up to 24 h. Patients in both groups showed a 100% stopping of the anti-blood-clotting effect of dabigatran when researchers analysed the maximum reversal within 4 hours.

In a few cases, re-bleeding or continuation of bleeding occurred. This required additional idarucizumab treatment. The figure on the next page shows the overall results.



What side effects did patients have?

Doctors noted side effects for 25 patients (5%) in the study during the first 5 days after they received idarucizumab. The most commonly reported side effects are shown in the table below.

	Total 503 patients
Total side effects	25 patients (5%)
Low blood pressure (hypotension)	3 patients (less than 1%)
Headache	2 patients (less than 1%)
Slow heartbeat (Bradycardia)	2 patients (less than 1%)

Doctors keep track of all health problems patients have during a study. In this study, most health problems were caused by the illness or emergency the patients had. Others might be caused by the study medicines, and some by other medicines taken by the patient. 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.

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

There were 6 patients (1%) who reported serious side effects during the 5-day on-treatment period. Two of these patients (less than 1%) had to stop taking the study medicine due to their serious side effects. One patient had a suspected case of anaphylactic shock. This is a serious allergic reaction causing difficulty in breathing or dizziness and was life-threatening. The other patient had slow heartbeat, low blood pressure, and low levels of oxygen in the blood. Other serious side effects were reported by 1 patient each. These were stroke, bleeding in the brain, heart attack, and heart stopped. Researchers from the sponsor of the study investigated these events. They found that these patients had other health problems that could also have caused these serious events.

Some patients had life-threatening illnesses or emergencies which were present prior to getting the study medicine. Many of these patients died due to these events, which were not caused by the study medicine. Over the entire study, 101 patients (20%) died. Doctors thought 5 deaths (1%) may have been 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: 1321.3
www.clinicaltrialsregister.eu	search for the EudraCT number: 2013-004813-41
www.clinicaltrials.gov	search for the NCT number: NCT02104947

The full title of the study is:

'A phase III, case series clinical study of the reversal of the anticoagulant effects of dabigatran by intravenous administration of 5.0 g idarucizumab (BI 655075) in patients treated with dabigatran etexilate who have uncontrolled bleeding or require emergency surgery or procedures. (RE-VERSE-AD trial: A study of the RE-VERSal Effects of idarucizumab on Active Dabigatran)'.

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.