This is a summary of a clinical study in patients with a heart rhythm disorder. 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 comparison of the safety of dabigatran and warfarin when combined with other anti-blood-clotting medicines in patients with a heart rhythm disorder who had just undergone a specific procedure called percutaneous coronary intervention'.

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

What was this study about?

In this study, researchers compared the safety of 2 types of medicine combinations that help to prevent blood from clotting. One of the combinations included dabigatran and the other included warfarin. These medicine combinations were given to patients with a special heart rhythm disorder called atrial fibrillation.

Many patients with atrial fibrillation also have problems with their arteries becoming plugged and have a higher risk of stroke. The patients in this study had just undergone a procedure called percutaneous coronary intervention (PCI) to open up an artery of the heart that was plugged. During the procedure, a short wire mesh tube (a stent) is moved into the place in the artery where the plug was. These patients required treatment with medicines that prevented their blood from clotting but also did not cause additional risks of serious bleeding. Researchers collected information on bleeding events and other side effects of these medicines.

This study started in August 2014 and finished in June 2017. The sponsor of this study was Boehringer Ingelheim.

Why was the study needed?

Patients with atrial fibrillation usually take anti-blood-clotting medicines regularly to prevent the risk of strokes. Such medicines are, for example, dabigatran and warfarin. When these patients have a PCI procedure, they need to take additional anti-blood-clotting medicines in combination with their regular medicines. These additional medicines are needed to prevent the formation of blood clots in the stent put in place during the PCI procedure. However, additional anti-blood-clotting medicines can also increase the risk of bleeding.

Doctors who treat these patients need to be able to balance the risk of stroke and blood clots with the risk of bleeding. If the risk of bleeding could be reduced, this would be an advantage for the patients.

Which medicines were studied?

Researchers studied combinations of the following 2 types of anti-blood-clotting medicines:

- Anticoagulant medicines, which slow down the clotting process and reduce the amount of certain proteins needed to form clots. In this study, these included dabigatran and warfarin.
- Antiplatelet medicines, which prevent small blood cells called platelets from forming clumps that are needed to form clots. In this study, these included clopidogrel, ticagrelor, and aspirin.

One combination was dabigatran and 1 antiplatelet medicine (clopidogrel or ticagrelor). This combination of 2 medicines is called dabigatran dual therapy. The other combination was warfarin and aspirin, plus 1 of the other antiplatelet medicines mentioned above. This combination of 3 medicines is called warfarin triple therapy.

Who participated in the study?

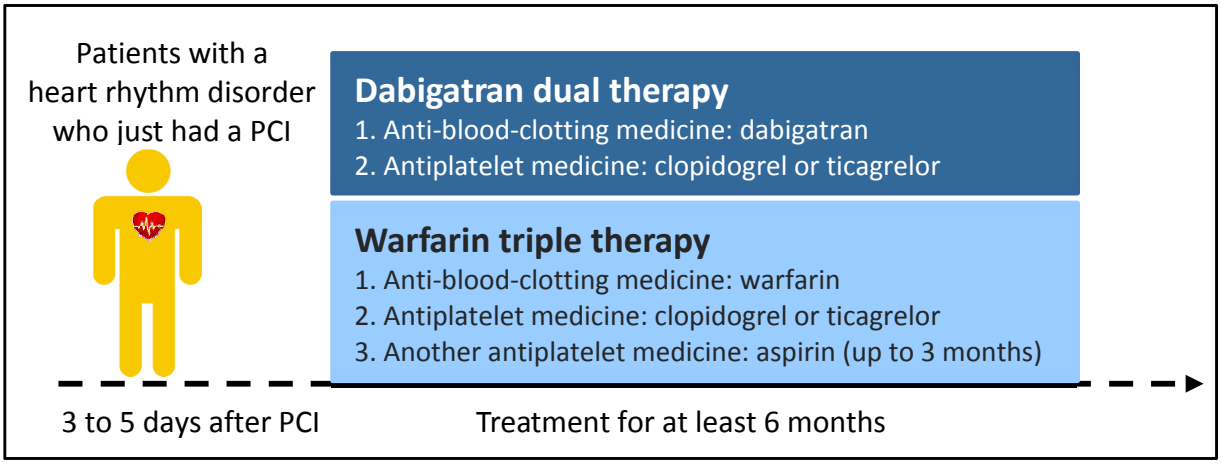
The patients in this study had a heart rhythm disorder called atrial fibrillation. They had just undergone PCI with stent placement within the past 5 days.

Overall, 2725 patients took part in the study: 2070 were men and 655 were women. On average, patients were 71 years old. The youngest patient was 29 years old and the oldest patient was 93 years old. The table below lists the regions and countries where these patients took part.

Geographical region	Countries	Patients
Western Europe	Austria, Belgium, Denmark, Finland, France, Germany, Greece, Italy, Ireland, Norway, Netherlands, Portugal, Spain, Sweden, United Kingdom	1308
Central Europe	Bulgaria, Croatia, Czech Republic, Hungary, Poland, Russia, Slovakia, Slovenia, Turkey	719
Asia	Hong Kong, India, Japan, Korea, Singapore, Taiwan, Thailand	313
North America	Canada, United States	199
Latin America	Argentina, Brazil, Chile, Colombia, Mexico	118
Other regions	Australia, Israel, New Zealand	68

How was this study done?

Patients were divided into groups to take either dabigatran dual therapy or warfarin triple therapy as shown in the figure below. It was decided by chance who took dabigatran dual therapy and who took warfarin triple therapy. Patients in the dabigatran dual therapy group were assigned to a lower dose of 110 milligrams (mg) or a higher dose of 150 mg, depending on their age. The dose of warfarin was determined by each patient's blood-clotting ability. The patients in the study and the study doctors knew which medicines the patients were taking.



Study medicines were started 6 hours to 5 days after the PCI with stent placement. Patients took 1 capsule of 110 milligrams (mg) of dabigatran twice daily, 1 capsule of 150 mg dabigatran twice daily, or warfarin once daily (the dose varied by patient). Patients also took 75 mg of clopidogrel once daily or 90 mg of ticagrelor twice daily. In the warfarin triple therapy group, patients also took aspirin once daily (the dose varied by patient). Dabigatran and warfarin were to be continued for at least 6 months. Clopidogrel and ticagrelor were to be continued for up to 12 months, and aspirin for up to 3 months.

Researchers compared the occurrence of major or clinically relevant bleeding events in each dabigatran group compared to the warfarin group. A bleeding event was considered major if at least 1 of the following occurred:

- The patient required a transfusion of blood.
- The bleeding occurred in an important place in the body (such as in the brain).
- The bleeding led to the death of the patient.

A bleeding event was considered clinically relevant if at least 1 of the following occurred:

- The patient was admitted to the hospital.
- The patient required treatment.
- The study doctor considered it necessary to change the dose or to stop the study drugs.

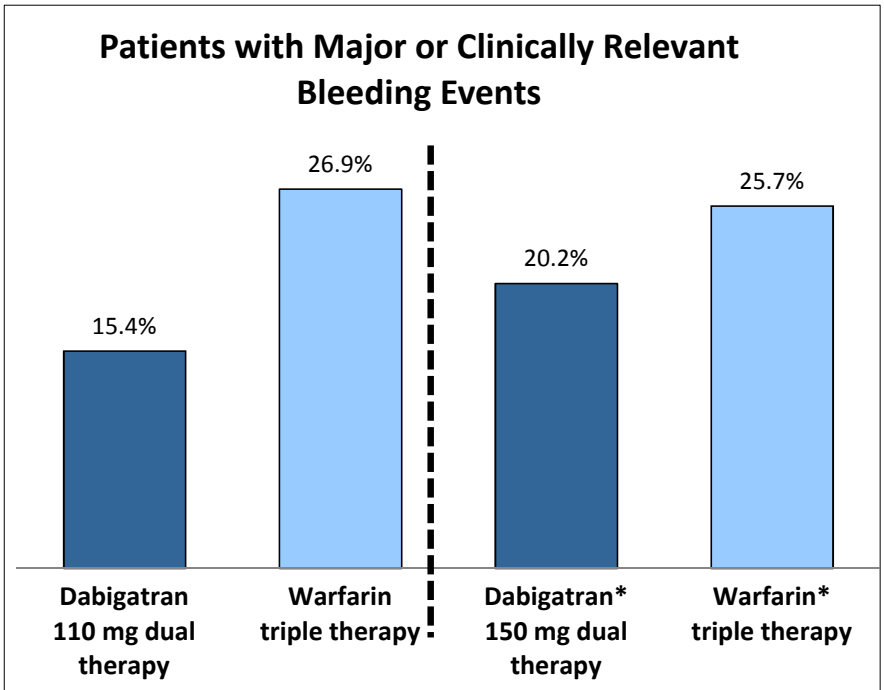
The study doctors checked carefully to see if the patients had bleeding events. If any bleeding event occurred, the doctor measured the time from starting the medicines until the event occurred.

Doctors also collected information on any other side effects.

What were the results of this study?

The percentage of patients with major or clinically relevant bleeding events was lower in the dabigatran dual therapy groups than in the warfarin triple therapy groups. A total of 15.4% of patients in the dabigatran 110 mg dual therapy group had bleeding events compared with 26.9% of patients in the warfarin triple therapy group. A total of 20.2% of patients in the dabigatran 150 mg dual therapy group had bleeding events compared with 25.7% of patients in the warfarin triple therapy group.

The picture below shows the percentage of patients in each group who had major or clinically relevant bleeding events.



This figure shows the percentage of patients with major or clinically relevant bleeding events in each treatment group. On average, the percentage of patients with bleeding events was lower in each of the dabigatran dual therapy groups than in the warfarin triple therapy groups.

*For the comparison, the only elderly patients included in these groups were from the United States.

The results show that dabigatran dual therapy lowered the risk of having bleeding events compared with warfarin triple therapy (relative risk reduction of 48% in 110 mg group and of 28% in 150 mg group). Researchers used statistical tests on the results and found that they were reliable.

What side effects did patients have?

In addition to the important bleeding events described above, all other side effects were also collected. Patients in each of the dabigatran dual therapy groups had fewer side effects than the patients in the warfarin triple therapy group. Overall, 24% of patients in the dabigatran 110 mg dual therapy group, 26% of patients in the dabigatran 150 mg dual therapy group, and 35% of patients in the warfarin triple therapy group had side effects.

The table below shows side effects that occurred in at least 2% of patients in any of the treatment groups.

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.

	Dabigatran 110 mg dual therapy (972 patients)	Dabigatran 150 mg dual therapy (758 patients)	Warfarin triple therapy (948 patients)
Patients with any side effect	230 patients (24%)	198 patients (26%)	335 patients (35%)
Nosebleed (Epistaxis)	42 patients (4%)	40 patients (5%)	115 patients (12%)
Swelling that is filled with blood (Haematoma)	19 patients (2%)	19 patients (3%)	43 patients (5%)
Blood in the urine (Haematuria)	17 patients (2%)	15 patients (2%)	22 patients (2%)
Upset stomach (Dyspepsia)	16 patients (2%)	10 patients (1%)	0 patients
Bruising (Contusion)	15 patients (2%)	11 patients (2%)	28 patients (3%)
Bleeding of the gums (Gingival bleeding)	9 patients (less than 1%)	14 patients (2%)	30 patients (3%)
Increased blood clotting time (INR increased)	0 patients	0 patients	29 patients (3%)
Bleeding under the skin (Subcutaneous haematoma)	6 patients (less than 1%)	2 patients (less than 1%)	19 patients (2%)

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. Or if it needed a doctor's immediate attention, was life-threatening, or caused death.

There were also fewer patients who had serious side effects in each of the dabigatran dual therapy groups than in the warfarin triple therapy group. A total of 55 patients (6%) in the dabigatran 110 mg dual therapy group and 40 patients (5%) in the dabigatran 150 mg dual therapy group had at least 1 serious side effect. In the warfarin triple therapy group, 85 patients (9%) had at least 1 serious side effect. The types of serious side effects were similar in the dabigatran and warfarin groups. The most common serious side effect was bleeding in the stomach (gastrointestinal haemorrhage).

A total of 38 patients (4%) in the dabigatran 110 mg dual therapy group, 24 patients (3%) in the dabigatran 150 mg dual therapy group, and 41 patients (4%) in the warfarin triple therapy group died during the study.

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: 1160.186
www.clinicaltrialsregister.eu	search for the EudraCT number: 2013-003201-26
www.clinicaltrials.gov	search for the NCT number: NCT02164864

The full title of the study is:

'A prospective randomised, open label, blinded endpoint (PROBE) study to evaluate dual antithrombotic therapy with dabigatran etexilate (110 mg and 150 mg b.i.d.) plus clopidogrel or ticagrelor vs. triple therapy strategy with warfarin (INR 2.0 – 3.0) plus clopidogrel or ticagrelor and aspirin in patients with non valvular atrial fibrillation (NVAF) that have undergone a percutaneous coronary intervention (PCI) with stenting (RE-DUAL PCI)'.

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.