# A study of heart safety in patients with type 2 diabetes and cardiovascular disease who are treated with empagliflozin (1245.25)

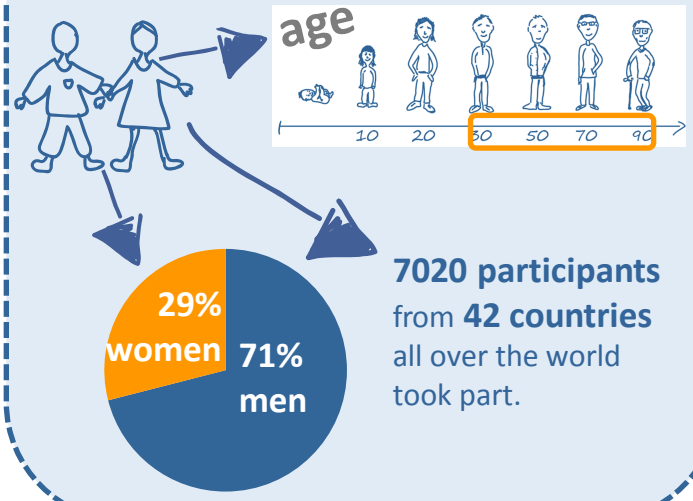
Boehringer Ingelheim

Patients with type 2 diabetes are more likely to get cardiovascular disease and to die from it.

This **study** was to find out:

Does **empagliflozin** increase or decrease the chance of having **serious cardiovascular problems in patients** with type 2 diabetes and cardiovascular disease?

## Participants who took part had type 2 diabetes and cardiovascular disease




**7020 participants** from **42 countries** all over the world took part.

Each participant took each day

1 10 mg or 25 mg empagliflozin

**or**

1 Placebo

in addition to their regular medication.

28% of participants who took empagliflozin and 24% of participants who took placebo had **unwanted effects.**


Hypoglycaemia was the most common unwanted effect with 13% (empagliflozin) and 12% (placebo).

## RESULTS

Participants taking empagliflozin had a smaller chance of getting serious cardiovascular problems than participants taking placebo. Empagliflozin lowered the chance of having a heart attack, a stroke, or dying due to cardiovascular disease by 14%. Empagliflozin lowered the chance of dying from cardiovascular disease by 38%.

# A study of heart safety in patients with type 2 diabetes and cardiovascular disease who are treated with empagliflozin

This is a summary of results from one clinical study.

We thank all study participants. You helped us to answer important questions about empagliflozin and the treatment of type 2 diabetes and cardiovascular disease.

## What was this study about?

The purpose of this study was to find out whether people with type 2 diabetes and cardiovascular disease who took a medicine called empagliflozin were more likely or less likely to have serious cardiovascular problems.

People with type 2 diabetes are more likely to have cardiovascular disease and to die from cardiovascular disease than from any other cause. Empagliflozin is a medicine that lowers blood sugar in patients with type 2 diabetes. It is important to find out whether medicines that are given to treat type 2 diabetes make cardiovascular disease more likely, or whether they may lower the risk of cardiovascular disease.

## Who took part in this study?

People who had type 2 diabetes and cardiovascular disease could take part in the study.

A total of 7020 participants were treated in the study. There were 5016 men (71% of participants) and 2004 women (29% of participants). The average age was 63 years. The youngest participant was 30 years old and the oldest was 90 years old.

The following table shows the numbers of participants in the study in different countries.

| Region | Countries | Number of Participants |
|---|---|---|
| Europe and Israel | Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, France, Georgia, Greece, Hungary, Israel, Italy, Netherlands, Norway, Poland, Portugal, Romania, Russia, Spain, Ukraine, United Kingdom | 2885 |
| North America and Western Pacific | Australia, Canada, New Zealand, United States | 1394 |
| Asia | Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Philippines, Singapore, Sri Lanka, Taiwan, Thailand | 1347 |
| Latin America | Argentina, Brazil, Colombia, Mexico, Peru | 1081 |
| Africa | South Africa | 313 |

## How was this study done?

The participants were divided into 3 groups of almost equal size. Every participant had an equal chance of being in each group. The groups were:

- Empagliflozin 10 mg group: participants took 1 tablet of 10 mg empagliflozin per day
- Empagliflozin 25 mg group: participants took 1 tablet of 25 mg empagliflozin per day
- Placebo group: participants took 1 tablet of placebo per day

Placebo tablets looked like empagliflozin but did not contain any medicine. We compared empagliflozin with placebo to find out about the effect of empagliflozin.

Participants were still taking all their usual medication (e.g. for type 2 diabetes or cardiovascular disease) as prescribed by their doctor.

The participants and doctors did not know whether the participants were in one of the empagliflozin groups or in the placebo group.

Participants in this study took empagliflozin or placebo tablets for about 2 years and 7 months on average.

Except for taking the different medicines, all participants followed the same procedures:

- Participants went to the study doctor every 4 to 14 weeks.
- Doctors took blood samples at certain visits.
- Doctors collected information on side effects at every visit.

- Participants had measurements of their heart rhythm taken at certain visits (electrocardiograms, or ECGs).

The doctors reviewed all medical test results at every visit. They discussed any health problems with the participants and performed further tests when needed.

The researchers wanted to know how many participants had a heart attack or a stroke, or died due to cardiovascular disease. Researchers call these events '3-MACE' which means 3 Major Adverse Cardiovascular Events. They combined the information from the 2 doses of empagliflozin to compare with placebo.

## What were the results of this study?

In the placebo group, 282 out of 2333 participants (12.1%) had a heart attack, a stroke, or died due to cardiovascular disease. In the empagliflozin groups, 490 out of 4687 participants (10.5%) had a heart attack, a stroke, or died due to cardiovascular disease. These results show that empagliflozin lowered the chance of having a heart attack, a stroke, or dying due to cardiovascular disease by 14%.

Researchers looked into more detail at each type of event that is included in 3-MACE: heart attacks, strokes, and death due to cardiovascular disease. The results showed that the main effect of empagliflozin was to lower the risk of dying from cardiovascular disease.

### How does empagliflozin affect the chances of dying from cardiovascular disease?

In the placebo group, 137 out of 2333 participants (5.9%) died due to cardiovascular disease. In the empagliflozin groups, 172 out of 4687 participants (3.7%) died due to cardiovascular disease. These results show that empagliflozin lowered the chance of dying from cardiovascular disease by 38%.

Researchers also looked at how many participants died in the study from any cause. In the placebo group, 194 out of 2333 participants (8.3%) died from any cause. In the empagliflozin groups, 269 out of 4687 participants (5.7%) died from any cause. These results show that participants who took empagliflozin had a 32% lower chance of dying from any cause than participants who took placebo.

### Does empagliflozin affect the chances of having a heart attack?

In the placebo group, 126 out of 2333 participants (5.4%) had a heart attack. In the empagliflozin groups, 223 out of 4687 participants (4.8%) had a heart attack. These results do not clearly show that there was any difference in the chance of having a heart attack between participants taking empagliflozin and participants taking placebo.

### Does empagliflozin affect the chances of having a stroke?

In the placebo group, 69 out of 2333 participants (3.0%) had a stroke. In the empagliflozin groups, 164 out of 4687 participants (3.5%) had a stroke. These results do not clearly show that there was any difference in the chance of having a stroke between participants taking empagliflozin and participants taking placebo.

## Did participants have any unwanted effects?

Yes, participants in the empagliflozin and placebo groups had unwanted effects. Unwanted effects are health problems that the doctors think were caused by empagliflozin or placebo. In this study, 1309 out of 4687 participants (28%) in the empagliflozin groups had unwanted effects. 549 out of 2333 participants (24%) in the placebo group had unwanted effects.

The table below shows the most common unwanted effects. The table also shows how many participants had each of these unwanted effects.

| **Type of unwanted effect** | **Empagliflozin (10 mg or 25 mg) 4687 participants were in this group** | **Placebo 2333 participants were in this group** |
|---|---|---|
| Low blood sugar (Hypoglycaemia) | 600 participants (13%) | 284 participants (12%) |
| Bladder infection (Urinary tract infection) | 226 participants (5%) | 120 participants (5%) |
| Frequent urination (Pollakiuria) | 65 participants (1%) | 15 participants (less than 1%) |
| Urinated large amounts of urine (Polyuria) | 50 participants (1%) | 9 participants (less than 1%) |

Some unwanted effects were serious because they required a visit to hospital or a longer stay in hospital, were life-threatening or fatal. Unwanted effects were also serious if they led to disability, or the doctor thought they were serious for any other reason. In this study,
93 participants (2%) in the empagliflozin groups had serious unwanted effects.
28 participants (1%) in the placebo group had serious unwanted effects.

## Where can I find more information about this study?

You can find further information about this study at these websites:

1. Go to http://www.trials.boehringer-ingelheim.com/ and search for the study number 1245.25
2. Go to www.clinicaltrialsregister.eu/ctr-search and search for the EudraCT number 2009-016178-33
3. Go to www.clinicaltrials.gov and search for the NCT number NCT01131676

Boehringer Ingelheim sponsored this study.

The full title of the study is: 'A Phase III, multicentre, international, randomised, parallel group, double blind cardiovascular safety study of BI 10773 (10 mg and 25 mg administered orally once daily) compared to usual care in type 2 diabetes mellitus patients with increased cardiovascular risk (The EMPA-REG OUTCOME® Trial)'

This study started in August 2010 and finished in April 2015.

## Are there additional studies?

If we do more clinical studies with empagliflozin you will find them on the websites listed above. To search for these studies, use the words empagliflozin and BI 10773.

## 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.