The EASE-2 study of empagliflozin in patients with type 1 diabetes

This is a summary of one clinical study. This summary describes the results of the study.

We thank all patients who took part in this study. You helped to answer important questions about empagliflozin and the treatment of type 1 diabetes.

What was this study about?

The purpose of this study was to find out whether a medicine called empagliflozin helps patients with type 1 diabetes who are using insulin.

Why was the study needed?

Patients with type 1 diabetes need to take insulin to control their blood sugar levels. But even with insulin, some patients are not able to control their blood sugar levels very well. Patients with type 1 diabetes can also have other problems like weight gain or hypoglycaemia. Hypoglycaemia is when blood sugar levels are too low. New medicines are needed to help patients with type 1 diabetes.

Which medicines were studied?

We studied a medicine called empagliflozin that is already used to treat type 2 diabetes. This medicine helps the kidneys remove sugar from the blood. The sugar is removed from the body in the urine. Empagliflozin is a tablet that patients swallow once a day.

We compared empagliflozin with placebo to find out how well empagliflozin works. Placebo tablets looked like empagliflozin but did not contain any medicine.

All patients in the study were already taking insulin. They continued to take insulin during the study.

Who participated in the study?

Adult patients with type 1 diabetes could take part in this study. They had to be at least 18 years old. They also had to have been taking insulin for at least 1 year before the start of the study.

Overall, 730 patients were treated in this study. There were 341 men and 389 women. The average age was 45 years. The youngest patient was 18 years old and the oldest was 77 years old.

The table below shows the number of patients in different regions who took part in the study.

Region	Countries	Number of Patients
Europe	Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Netherlands, Norway, Poland, Spain, Sweden, United Kingdom	399
North America	Canada, United States	282
Pacific	Australia	32
Asia	Taiwan	17

How was this study done?

The study started with a 6-week period during which the study doctors paid special attention to each patient's diabetes treatments. They checked that each patient was getting the best possible insulin dose.

The patients were then divided into 3 groups of almost equal size. Every patient had an equal chance of being in a certain group. The groups were:

Empagliflozin 10 mg group: patients took 1 tablet of 10 mg empagliflozin per day

Empagliflozin 25 mg group: patients took 1 tablet of 25 mg empagliflozin per day

Placebo group: patients took 1 placebo tablet per day

The treatment was taken for 52 weeks. The patients and the study doctors did not know in which group the patients were. All patients continued their insulin treatment during the study.

During the study, the doctors did a measurement called HbA_{1c}. This is a measure of how much sugar on average was in the blood over the last 12 weeks. We wanted to know how much the blood sugar levels changed after 26 weeks of treatment.

Patients visited the study doctors regularly. During these visits, the study doctors collected information about the patient's health. The doctors also checked the patients for any unwanted effects. They also looked for signs of diabetic ketoacidosis. Ketoacidosis is a serious complication that can affect patients with type 1 diabetes.

What were the results of this study?

For 6 weeks before the study, the study doctors checked that each patient got the best possible insulin dose. During this time, the blood sugar control of the patients improved. The patients then started treatment with empagliflozin or placebo.

After 26 weeks of treatment, both doses of empagliflozin led to further reductions in HbA_{1c}. This means that the patients who took empagliflozin further improved their blood sugar control. But for patients who took placebo, there was no improvement in blood sugar control. For these patients, HbA_{1c} increased after 26 weeks.

To measure how well the treatment worked, we calculated the changes in HbA_{1c} in all 3 groups, (10 mg, 25 mg empagliflozin groups and the placebo group). Taking the placebo group as a reference, we found the following reductions in HbA_{1c}:

- In the 10 mg empagliflozin group, the reduction was 0.54%
- In the 25 mg empagliflozin group, the reduction was 0.53%

In the 10 mg and 25 mg empagliflozin groups, there were also more cases of ketoacidosis than in the placebo group. 15 patients (6.2%) in the empagliflozin 10 mg group and 10 patients (4.1%) in the empagliflozin 25 mg group had ketoacidosis. 3 patients (1.2%) in the placebo group had ketoacidosis.

Another problem that people with diabetes sometimes have is hypoglycaemia. This means that the blood sugar level falls too low. In this study, we checked how many patients had hypoglycaemia. We found that patients who took empagliflozin did not have more hypoglycaemia than patients who took placebo.

People with type 1 diabetes tend to gain weight easily. It can also be difficult for them to lose weight. The patients who took the 10 mg and 25 mg doses of empagliflozin lost an average of about 3 kg of body weight. Patients who took placebo did not lose weight.

Were there any unwanted effects?

Unwanted effects are any health problems that the doctors thought were caused by empagliflozin or placebo. In this study after 52 weeks, 127 out of 243 patients (52%) treated with empagliflozin 10 mg had unwanted effects. 130 out of 244 patients (53%) treated with empagliflozin 25 mg had unwanted effects. 102 out of 243 patients (42%) treated with placebo had unwanted effects. The most common unwanted effects seen in at least 5% of patients in any of the treatment groups are shown in the table below.

	Empagliflozin 10 mg (243 patients)	**Empagliflozin 25 mg (244 patients)**	**Placebo (243 patients)**
Too little sugar in the blood (hypoglycaemia)	74 patients (31%)	66 patients (27%)	66 patients (27%)
Urinary tract infection	23 patients (10%)	15 patients (6%)	18 patients (7%)
Higher levels of ketones in the blood (blood ketone body increased)	13 patients (5%)	14 patients (6%)	6 patients (3%)

Some unwanted effects were serious because they required a visit to or a longer stay in hospital, or were life-threatening. Unwanted effects were also serious if the doctor thought they were serious for any other reason. In this study after 52 weeks, 19 patients (8%) treated with 10 mg empagliflozin had serious unwanted effects. 10 patients (4%) treated with 25 mg empagliflozin had serious unwanted effects. 5 patients (2%) treated with placebo had serious unwanted effects.

Are there additional studies?

If researchers do additional clinical studies with empagliflozin, you will find them on the websites listed in the next section. To search for these studies, use the following names: BI 10773, empagliflozin.

Where can I find more information?

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

1. Go to http://www.trials.boehringer-ingelheim.com/ and search for the study number BI 1245.69.
2. Go to www.clinicaltrialsregister.eu/ctr-search and search for the EudraCT number 2014-001922-14.
3. Go to www.clinicaltrials.gov and search for the NCT number NCT02414958.

Boehringer Ingelheim sponsored this study.

The full title of the study is: 'A Phase III, randomised, double blind, placebo-controlled, parallel group, efficacy, safety and tolerability trial of once daily, oral doses of Empagliflozin as Adjunctive to inSulin thErapy over 52 weeks in patients with Type 1 Diabetes Mellitus (EASE-2)'.

This study started in July 2015 and finished in October 2017.

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.