This is a summary of a clinical study in type 2 diabetes. 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 'MARLINA-T2D: Efficacy, Safety and Modification of Albuminuria in Type 2 Diabetes Patients with Kidney Disease with Linagliptin'.

We thank all patients who took part in this study. Through your participation, you helped researchers answer important questions about linagliptin and the treatment of type 2 diabetes.

What was this study about?

This study tested a medicine called linagliptin to treat patients with type 2 diabetes who also had too much protein in their urine (albuminuria). Researchers wanted to see how well the medicine worked when taken for 24 weeks in this group of patients. They also wanted to know what side effects there were, and how well patients tolerated the medicine.

The study started in February 2013 and ended in December 2015. The sponsor of this study was Boehringer Ingelheim.

Why was the study needed?

Patients with type 2 diabetes have too much sugar in their blood. This can increase the risk of serious medical problems such as heart or kidney disease. Therefore, controlling blood sugar levels is important for patients with type 2 diabetes.

Patients may be able to control their blood sugar levels by following a diet and exercise plan. Sometimes, patients need medicine to treat their type 2 diabetes. There is a need to develop medicines that allow patients to control their blood sugar levels over long periods of time with fewer side effects.

This study tested whether taking linagliptin helped control blood sugar levels.

Which medicines were studied?

The name of the medicine studied was linagliptin. It helps the pancreas make more insulin. The pancreas is a gland in your abdomen. It aids in digestion and regulates how much sugar is available for your body. More insulin in the blood lowers blood sugar levels. Linagliptin also lowers the amount of sugar the liver makes. The study compared linagliptin to placebo. The placebo was a tablet that looked like the linagliptin tablet but had no active medicine in it. Patients were supposed to take a tablet by mouth each day for 24 weeks.

Who participated in the study?

The study included patients with type 2 diabetes who also had too much protein in their urine. Most patients were taking 1 or 2 oral medicines for their type 2 diabetes. Patients were also taking medicines to limit high protein in urine and to treat high blood pressure. Their diabetes medicines were taken at a stable dose that was not changed while they were in the study. The average age was 61 years old. The youngest patient was 29 years old, and the oldest was 80 years old. There were 229 men (64%) and 131 women (36%) in the study.

Patients could be in the study if they had:

- A glycated haemoglobin (HbA_{1c}) level from 6.5% to 10.0% at the start of the study
- Too much protein in their urine (albuminuria)
- Followed a diet and an exercise plan

Overall, 360 patients were treated in the study. The table below lists the regions and countries where patients took part in the study.

Asia (228 patients):

Japan	Taiwan
Korea	Vietnam
Philippines	

Europe (67 patients):

Denmark	Germany
Finland	Spain
France	

North America (65 patients):

Canada
United States

How was this study done?

The researchers wanted to know how linagliptin affected the amount of sugar in the blood. To do this, they measured the amount of a protein called glycated haemoglobin (HbA_{1c}) in the blood. Doctors measure HbA_{1c} levels to see how controlled a patient's blood sugar level has been over the past 3 months. Patients whose blood sugar is not controlled have high HbA_{1c} levels.

The researchers measured the patients' HbA_{1c} levels at the beginning of the study. Researchers also measured the HbA_{1c} levels during the 24 weeks of treatment. The researchers wanted to know how much the patients' HbA_{1c} levels changed after 24 weeks of treatment. In addition, researchers collected information on the side effects of the study medicines.

Patients in this study were randomly assigned to 1 of 2 treatment groups of similar size. One group of patients took linagliptin (5-milligram tablets). The other group of patients took a placebo. The placebo was a tablet that looked like the linagliptin tablet but had no active medicine in it. It was decided by chance who got into which group. Neither the

patients nor the study doctors knew which study medicine the patients got. The patients in each group took the following study medicine by mouth once each day for 24 weeks:

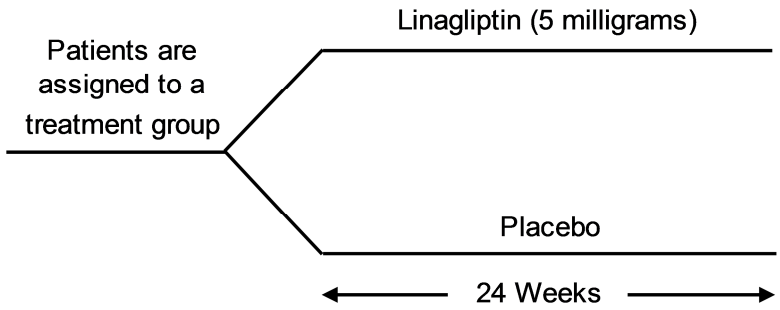
Linagliptin group: 1 tablet (5 milligrams)

Placebo group: 1 tablet

All patients had to follow similar procedures:

- Patients took their study medicine once per day for 24 weeks.
- Patients went to the study doctor every 4 to 6 weeks.
- Doctors took blood samples at specific visits.
- Doctors collected information on side effects.
- Patients answered questions about their health.
- Doctors reviewed the blood test results. They also discussed any health problems with the patients and performed further medical tests when needed.

The study design is shown in the figure below.



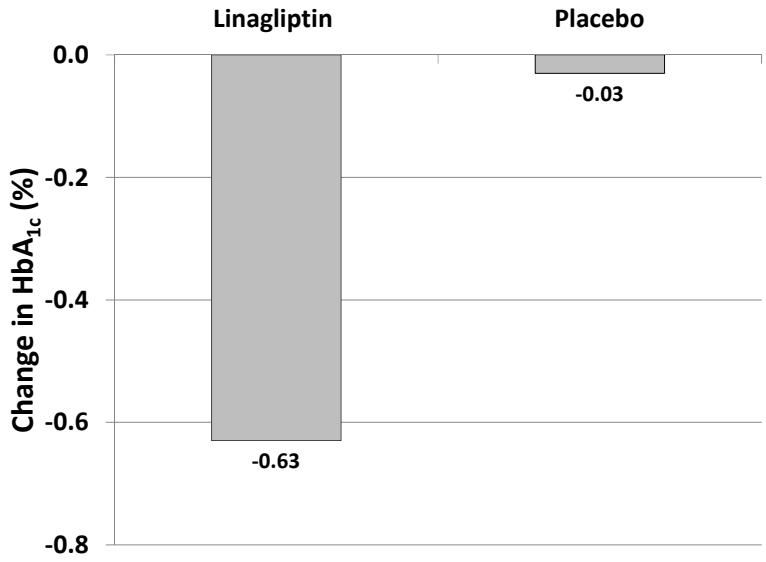
What were the results of this study?

The researchers compared the patients' HbA_{1c} levels at the beginning of the study with their levels after 24 weeks of treatment with linagliptin or placebo.

Was there a greater reduction of HbA_{1c} in patients who took linagliptin?

Yes. There was a greater reduction in the HbA_{1c} level in patients who took linagliptin than in patients who took placebo. Researchers used statistical tests on the results. Using these tests, they found that the difference in results between the treatment groups was not likely due to chance.

The picture below shows how the average (mean) HbA_{1c} level changed from before study treatment started to the end of 24 weeks of treatment.



This picture shows the average (mean) change in HbA_{1c} level at the end of 24 weeks of treatment. The HbA_{1c} level decreased by 0.63% in patients who took linagliptin over 24 weeks. The HbA_{1c} level decreased by 0.03% in patients who took placebo. There was a difference of −0.60% between the 2 treatment groups.

Which side effects did patients have?

The number of side effects was similar for each treatment group. About 7% of patients taking linagliptin and 6% of patients taking placebo had at least 1 side effect. Patients who took linagliptin were more likely to have low blood sugar levels (10 patients, or 6%) than patients who took placebo (2 patients, or 1%).

The table below shows the side effects that occurred in more than 1 patient in either treatment group.

	Linagliptin (182 patients)	**Placebo (178 patients)**
Patients with any side effect	13 patients (7%)	11 patients (6%)
Low blood sugar (Hypoglycaemia)	10 patients (6%)	2 patients (1%)
High pancreatic enzyme (Increased lipase)	1 patient (less than 1%)	2 patients (1%)

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.

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.

Most side effects were mild or moderate in their intensity. Three patients (2 patients in the placebo group and 1 patient in the linagliptin group) had a serious side effect. Two patients (1 patient in the placebo group, 1 patient in the linagliptin group) left the study early because of serious side effects. Three patients died during the study (1 patient in the placebo group, 2 patients in the linagliptin group). The study doctors determined that none of these deaths were 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: 1218.89
www.clinicaltrialsregister.eu	search for the EudraCT number: 2012-002603-17
www.clinicaltrials.gov	search for the NCT number: NCT01792518

The full title of the study is:

'A phase IIIb, multicentre, multinational, randomized, double-blind, placebo controlled, parallel group study to evaluate the glycemic and renal efficacy of once daily administration of linagliptin 5 milligrams for 24 weeks in type 2 diabetes patients, with micro- or macroalbuminuria (30-3000 milligrams/gram creatinine) on top of current treatment with Angiotensin Converting Enzyme inhibitor or Angiotensin Receptor Blocker – MARLINA (Efficacy, safety & Modification of Albuminuria in type 2 diabetes subjects with Renal disease with LINAgliptin)'.

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.