

Effect of linagliptin on cardiovascular health and kidney function in patients with type 2 diabetes who have cardiovascular risks (the CARMELINA study, 1218.22)

People with **type 2 diabetes**

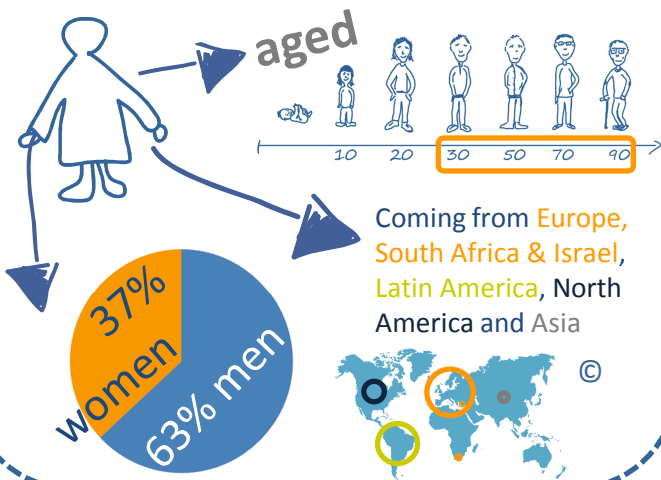
have a 2- to 4-fold higher risk of cardiovascular disease. *

This **study** tested linagliptin on top of standard care in patients with type 2 diabetes.



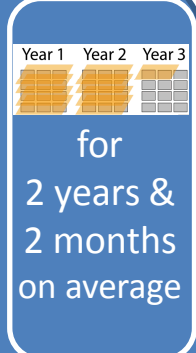
Is linagliptin as safe as placebo if added to one's standard meds in regards to heart attack or stroke or cardiovascular death?

Patients taking part were at risk of cardiovascular diseases



Each patient took each day

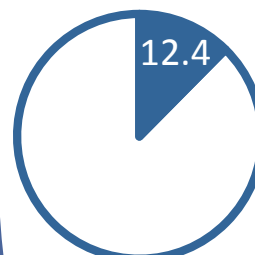
1 5 mg Linagliptin
or
1 Placebo
which didn't contain active medicine



RESULTS

The percentage of patients with heart attack or stroke or cardiovascular death was **similar** for linagliptin and placebo.

Linagliptin



Placebo

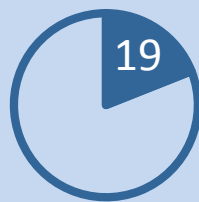


Percent of patients

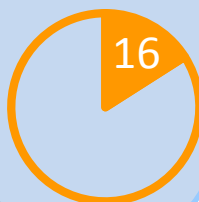
A similar percentage of patients in the linagliptin group and in the placebo group experienced **unwanted effects**.



Linagliptin



Placebo



Percent of patients

* See Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. N Engl J Med 1998;339(4):229-234. Emerging Risk Factors Collaboration. Lancet. 2010;375(9733):2215-2222. World map ©Fotolia by Maeliss

CARMELINA: Effect of linagliptin on cardiovascular health and kidney function in patients with type 2 diabetes who have cardiovascular risks

This is a summary of a clinical study in type 2 diabetes. It describes how researchers did the study and what the results were. We have written this summary for the general public.

Thank you for taking part in this study. By taking part in this study, you helped researchers answer important questions about linagliptin and the treatment of type 2 diabetes.



What was this study about?

This was a study in patients with type 2 diabetes. Researchers wanted to find out if patients taking linagliptin were more likely or not to have serious cardiovascular problems.



Why was this study needed?

Patients with type 2 diabetes are more likely to have cardiovascular disease and to die from cardiovascular disease than from any other cause. It is important to find out whether medicines given for type 2 diabetes have an effect on the risk of cardiovascular disease.



Which medicines were studied?

Researchers studied a medicine called linagliptin. Linagliptin is used to treat type 2 diabetes. It is a tablet that is taken by mouth.

Placebo tablets looked like linagliptin but did not contain any medicine. Researchers compared linagliptin with placebo.

Patients continued to get treatment with their usual medicines for type 2 diabetes, cardiovascular disease, or kidney disease as needed.



Who took part in this study?

Patients who had type 2 diabetes and cardiovascular disease, kidney disease, or both could take part in the study.

Overall, 6979 patients were treated in this study. There were 4390 men (63% of patients) and 2589 women (37%). The average age was 66 years. The youngest patient was 27 years old. The oldest patient was 92 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	Bulgaria, Croatia, Czech Republic, Germany, Hungary, Israel, Netherlands, Poland, Portugal, Romania, Russia, South Africa*, Spain, Ukraine, United Kingdom	2936
Latin America	Argentina, Brazil, Chile, Colombia, Mexico	2314
North America	Canada, United States	1183
Asia	China, Japan, Malaysia, South Korea, Taiwan	558

*For this study, data from South Africa was analysed with data from European countries.



How was this study done?

Patients were divided into 2 groups of nearly equal size. Every patient had an equal chance of being in each group. The patients did not know which treatment they were taking. The doctors did not know either.

The patients in each group took one of the following medicines every day:

Linagliptin group: 1 tablet containing 5 mg of linagliptin

Placebo group: 1 placebo tablet

Patients in this study took linagliptin or placebo tablets for about 2 years and 2 months on average. During the study, patients continued to take their usual medicines.

Patients visited their doctors regularly. During the visits, the doctors collected information on each patient's health.

Researchers wanted to know how many patients had at least 1 of 3 cardiovascular events. The events were heart attack, stroke, or death due to cardiovascular disease. Researchers call these events '3-MACE', which means 3 major adverse cardiovascular events.



What were the results of this study?

Patients taking linagliptin had no more of a risk of having a heart attack or stroke than patients taking placebo.















In the placebo group, 420 out of 3485 patients (12.1%) had a heart attack, a stroke, or died due to cardiovascular disease. In the linagliptin group, 434 out of 3494 patients (12.4%) had a heart attack, a stroke, or died due to cardiovascular disease. In the placebo group, 373 out of 3485 patients (10.7%) died. In the linagliptin group, 367 out of 3494 patients (10.5%) died.




Were there any unwanted effects?

Unwanted effects are any health problems that the doctors thought were caused by the study medicines. In this study, 647 out of 3494 patients (19%) taking linagliptin had unwanted effects. 562 out of 3485 patients (16%) taking placebo had unwanted effects.

The most common unwanted effects seen in at least 10 patients taking either linagliptin or placebo are shown in the table below.

	Linagliptin (5 mg) (3494 patients) 	Placebo (3485 patients) 
Too little sugar in the blood (hypoglycaemia)	425 patients (12%) 	378 patients (11%) 
Too much of a pancreatic enzyme (lipase increased)	50 patients (1%) 	22 patients (1%) 
Too much sugar in the blood (hyperglycaemia)	17 patients (1%) 	29 patients (1%) 
Reduced kidney function (glomerular filtration rate decreased)	13 patients (less than 1%) 	16 patients (1%) 
Diarrhoea	12 patients (less than 1%) 	5 patients (less than 1%) 
Dizziness	7 patients (less than 1%) 	11 patients (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. During this study, 83 patients (2%) in the linagliptin group had serious unwanted effects. 68 patients (2%) in the placebo group had serious unwanted effects.



Are there additional studies?

If researchers do additional clinical studies with linagliptin, you will find them on the websites listed in the next section. To search for these studies, use the following names: linagliptin, BI 1356.

No additional studies are currently planned for the patients with type 2 diabetes who took part in this study with linagliptin.



Where can I find more information about this study?

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 1218.22.
2. Go to www.clinicaltrialsregister.eu/ctr-search and search for the EudraCT number 2011-004148-23.
3. Go to www.clinicaltrials.gov and search for the NCT number NCT01897532.

Boehringer Ingelheim sponsored this study.

The full title of the study is: 'A multicenter, international, randomized, parallel group, double-blind, placebo-controlled Cardiovascular Safety & Renal Microvascular outcome study with LINAgliptin, 5 mg once daily in patients with type 2 diabetes mellitus at high vascular risk. CARMELINA'.

This was a Phase 4 study. This study started in July 2013 and finished in January 2018.

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.

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