

## CAROLINA: Comparison of the effects of linagliptin and glimepiride on cardiovascular health in patients with type 2 diabetes who have cardiovascular risks (1218.74)

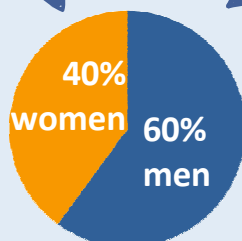
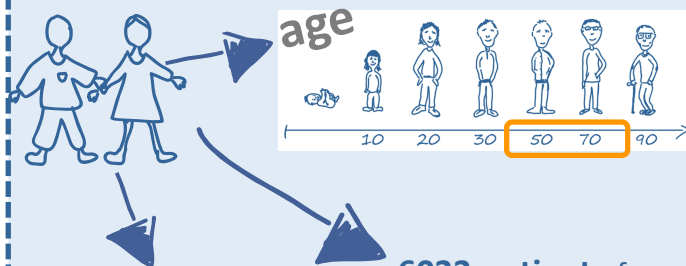
Patients with **type 2 diabetes** are more likely to have **cardiovascular disease** and to die from it.

This **study** was to find out:





Are patients taking a medicine called **linagliptin** no more likely to have **serious cardiovascular problems** than patients taking a medicine called **glimepiride**?

**Patients who took part had type 2 diabetes and an increased risk of cardiovascular disease**



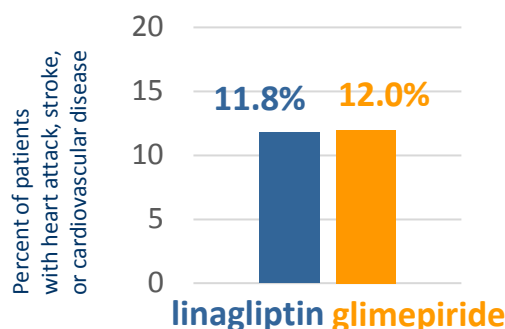
**6033 patients** from **43 countries** all over the world took part.

Each patient took each day

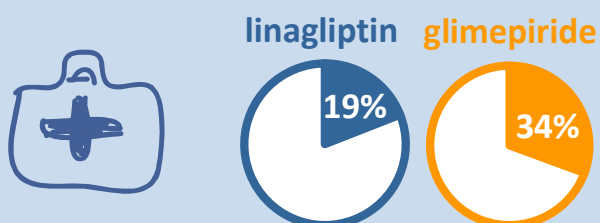
1  5 mg linagliptin  
or  
1  1 to 4 mg glimepiride

## RESULTS

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



19% of patients who took linagliptin and 34% of patients who took glimepiride had **unwanted effects**.



Hypoglycaemia was the most common unwanted effect with 5% (linagliptin) and 24% (glimepiride).

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## CAROLINA: Comparison of the effects of linagliptin and glimepiride on cardiovascular health in patients with type 2 diabetes who have cardiovascular risks

This is a summary of results from one clinical study.

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

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### What was this study about?

The purpose of this long-term study was to test a medicine called linagliptin as a treatment for type 2 diabetes. Patients taking linagliptin were compared to patients taking a medicine called glimepiride. We wanted to find out whether 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. It is important to find out if medicines given for type 2 diabetes have an effect on the risk of cardiovascular disease.



### Which medicines were studied?

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

We compared linagliptin to glimepiride, another medicine that is used to treat type 2 diabetes. Glimepiride is a tablet that is taken by mouth.



### Who took part in this study?

Patients who had type 2 diabetes and an increased risk of cardiovascular disease could take part in the study.

Overall, 6033 patients were treated in this study. There were 3619 men (60% of patients) and 2414 women (40% of patients). The average age was 64 years. The youngest patient was 36 years old and the oldest patient was 85 years old.

This study was done in Europe; North America, New Zealand, and Australia; Asia; South America and Mexico; and Africa. The table below shows the countries that the study was done in.

Region	Countries	Number of Patients
Europe	Belgium, Bulgaria, Czech Republic, Finland, France, Georgia, Germany, Greece, Hungary, Ireland, Israel*, Italy, Netherlands, Norway, Portugal, Romania, Russia, Serbia, Slovakia, Spain, Sweden, Switzerland, Ukraine, United Kingdom	2821
North America, New Zealand, and Australia	Australia, Canada, New Zealand, United States	1240
Asia	Hong Kong, India, Japan, Korea, Malaysia, Philippines, Taiwan	933
South America and Mexico	Argentina, Brazil, Chile, Colombia, Mexico, Peru	908
Africa	South Africa, Tunisia	131

\*Patients in Israel were counted together with patients in Europe.



## 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

**Glimepiride group:** 1 tablet containing 1 mg, 2 mg, 3 mg, or 4 mg of glimepiride

Patients in this study took linagliptin or glimepiride tablets for about 5 years and 10 months on average. During the study, patients continued to take their usual medicines for type 2 diabetes or cardiovascular disease as needed.

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

We wanted to know how many patients had at least 1 of 3 major cardiovascular events. The term to describe this is '3P-MACE'. The events were heart attack, stroke, or death due to cardiovascular disease. If a patient had more than one of these events, we looked at the first event for calculating the main results of the study.



## What were the results of this study?

Patients taking linagliptin had no more of a risk of having a heart attack or a stroke than patients taking glimepiride. Patients taking linagliptin also had no more of a risk of dying from cardiovascular disease than patients taking glimepiride.













In the linagliptin group, 356 out of 3023 patients (11.8%) had a heart attack, a stroke, or died due to cardiovascular disease. In the glimepiride group, 362 out of 3010 patients (12.0%) had a heart attack, a stroke, or died due to cardiovascular disease.



## Did patients have any unwanted effects?

Yes, patients in both groups had unwanted effects. Unwanted effects are health problems that the doctors think were caused by linagliptin or glimepiride. In this study, 584 out of 3014 patients (19%) taking linagliptin had unwanted effects. 1021 out of 3000 patients (34%) taking glimepiride had unwanted effects.

The table below shows the 5 most common unwanted effects.

Unwanted effect	Linagliptin (3014 patients)		Glimepiride (3000 patients)	
Hypoglycaemia (too little sugar in the blood)	159 patients (5%)		708 patients (24%)	
Too much of an enzyme called lipase	78 patients (3%)		50 patients (2%)	
Too much of an enzyme called amylase	49 patients (2%)		33 patients (1%)	
Hyperglycaemia (too much sugar in the blood)	39 patients (1%)		49 patients (2%)	
Dizziness	22 patients (1%)		53 patients (2%)	

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, 49 patients (2%) in the linagliptin group had serious unwanted effects. 55 patients (2%) in the glimepiride group had serious unwanted effects.



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

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

1. Go to <http://www.trials.boehringer-ingelheim.com/> and search for the study number BI 1218.74.
2. Go to [www.clinicaltrialsregister.eu/ctr-search](http://www.clinicaltrialsregister.eu/ctr-search) and search for the EudraCT number 2009-013157-15.
3. Go to [www.clinicaltrials.gov](http://www.clinicaltrials.gov) and search for the NCT number NCT01243424.

Boehringer Ingelheim sponsored this study.

The full title of the study is: 'A multicentre, international, randomised, parallel group, double blind study to evaluate Cardiovascular safety of linagliptin versus glimepiride in patients with type 2 diabetes mellitus at high cardiovascular risk. The CAROLINA Trial'.

This was a Phase 3 study. This study started in November 2010 and finished in August 2018.



## Are there additional studies?

If we do more clinical studies with linagliptin, you will find them on the websites listed above. To search for these studies, use the words linagliptin or BI 1356.

## 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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