Results from a study looking at whether insulin resistance affects how well finerenone works to treat patients with chronic kidney disease and type 2 diabetes

Date of Summary: March 2024

The purpose of this plain language summary is to help you understand the results from a recent extra analysis from the FIDELITY study.

- Finerenone is approved to treat chronic kidney disease (CKD) in people who also have type 2 diabetes (T2D)
- Researchers must look at the results of many studies to understand if a study drug works, how it works, and whether it is safe for patients to take
- The FIDELITY study combined results from two other studies called FIDELIO-DKD and FIGARO-DKD, with the aim of finding out how well finerenone works in reducing the chance of heart and kidneys problems in a much larger sample of people with CKD and T2D
- This summary looks at the results of an extra analysis that was done using data from FIDELITY after the main FIDELITY study had been completed

PHONETICS

Finerenone: <fin-er-e-none>

Hyperkalemia: <hai-puh-kuh-lee-mee-uh>

Mineralocorticoid receptor antagonist: <min-er-alo-cor-ti-coid ruh-sep-tuh an-ta-guh-nuhst>

What did this study look at?

- Medicines for treating CKD aim to slow how quickly CKD gets worse
- Having CKD also increases the chance of developing heart problems, so medicines for CKD may also help to reduce the risk of heart problems
- This extra analysis from the FIDELITY study looked at whether having insulin resistance makes people with CKD and T2D more likely to develop heart problems and worsening kidney problems. It also looked at whether insulin resistance changes how well finerenone works as a treatment for people with CKD and T2D

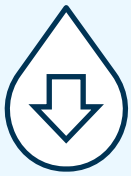
What is type 2 diabetes and chronic kidney disease?

Example of normal response to high blood glucose levels

1. High blood glucose levels

2. Cause the pancreas to release **insulin** into the blood

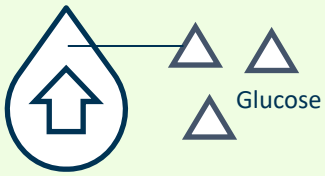
3. Insulin causes glucose-storing cells in the body to take in glucose from the blood



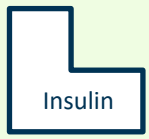
4. Reduction in blood glucose levels

Example of normal response to high blood glucose levels such as may happen after eating a large starchy meal

Example of insulin resistance leading to ongoing high glucose levels



1. High blood glucose levels



2. Cause the pancreas to release **insulin** into the blood

3. Cells that normally take in glucose become insensitive (resistant) to insulin

4. Blood glucose levels stay high

Insulin resistance increases a person's risk of developing type 2 diabetes. If blood glucose levels are too high, over a long period of time, this can cause other health conditions, including heart and kidney problems

- Around 1 in 3 people with T2D in the United States will develop a kidney condition called CKD

What is finerenone?

- Finerenone is a medicine used to treat people with CKD and T2D. It is a tablet that is taken once a day
- Finerenone works by reducing inflammation, which reduces the risk of further kidney damage and heart problems

What did researchers look at in this study?

- In the main FIDELITY study, researchers wanted to find out how well finerenone effects the heart and kidneys in a large sample of people with CKD and T2D
- In this extra analysis using data from the FIDELITY study, researchers wanted to find out if having insulin resistance makes people with CKD and T2D more likely to have heart problems or have worsening kidney problems
- The researchers also wanted to know if having insulin resistance changed how well finerenone worked in people with CKD and T2D
- The researchers also looked at what side effects people in the study had

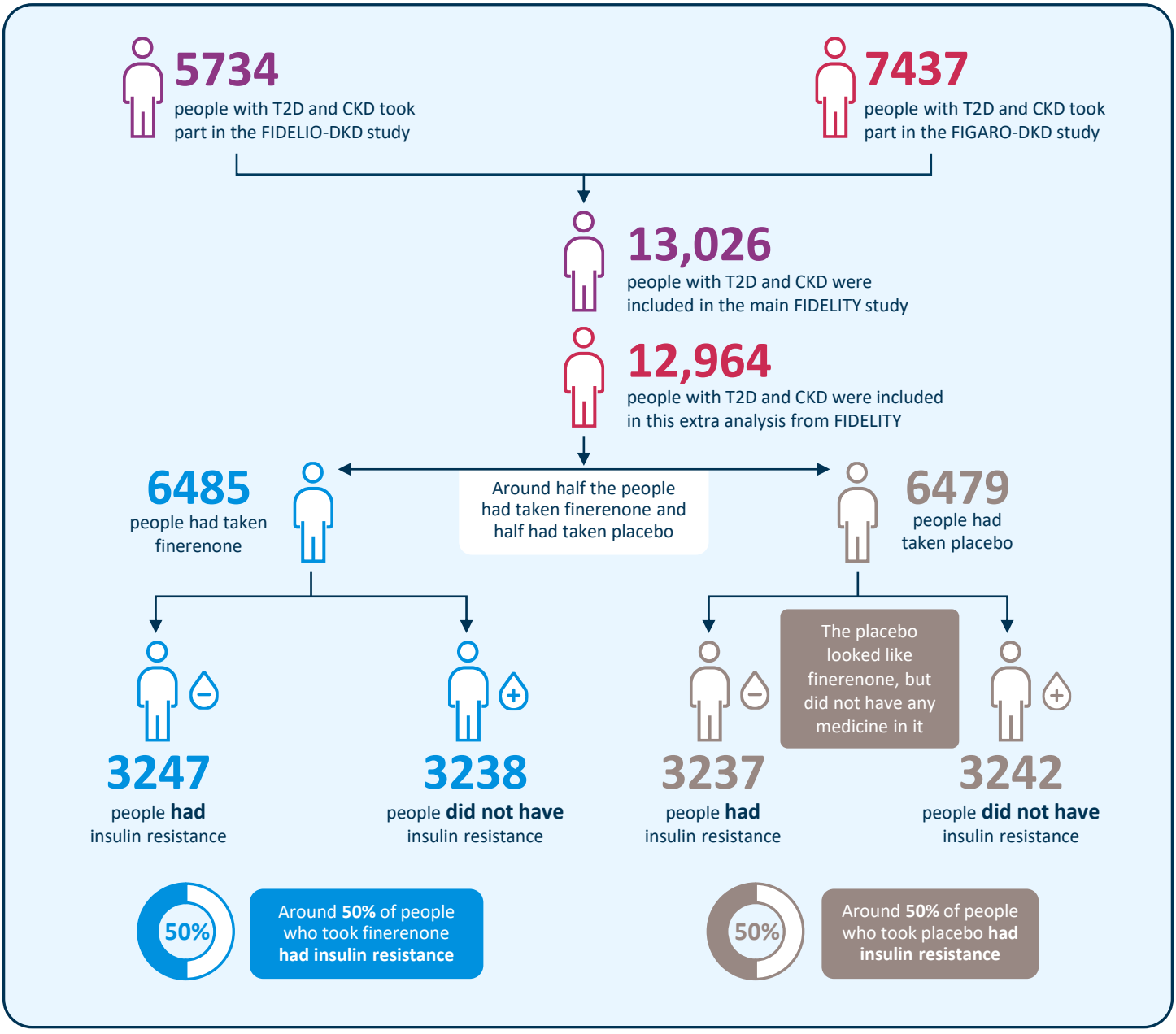
Who took part in the study?

People in the FIDELITY study had already taken part in one of two earlier studies:

- **FIDELIO-DKD**: a study that looked at how well finerenone could reduce the chance of kidney failure and other associated kidney problems in people with T2D and CKD
- **FIGARO-DKD**: a study that looked at how well finerenone could reduce the chances of heart problems in people with T2D and CKD

People who took part in the FIDELITY study were:

- At least 18 years old
- Had CKD and T2D
- Were taking a type of medicine that has effects, including helping to regulate blood pressure
- On average, people took part in the study for 3 years



What were the researchers interested in finding out from the main FIDELITY study?

The researchers were interested in looking at the effects of finerenone on heart events and kidney events

Heart events

What heart outcomes did the researchers look at?

The researchers looked at people in the study who:

- Died because of their heart disease
- Had a heart attack (but did not die)
- Had a stroke (but did not die)
- Had to go to hospital due to heart failure

They wanted to know how long it was from the start of the study until people had any of these outcomes

They combined all of these outcomes into one measure to work out the chance of people having heart events after 3.5 years

Kidney events

What kidney outcomes did the researchers look at?

The researchers looked at people in the study:

- Who started to develop kidney failure
- Whose kidney function got worse by 57% or more in 1 month
- Who had kidney failure

They wanted to know how long it was from the start of the study until people had any of these outcomes

They combined all of these outcomes into one measure to work out the chance of people having kidney events after 3.5 years

What were the researchers interested in finding out from the extra analysis from the FIDELITY study?

The researchers were interested in looking at the effects of finerenone on heart events and kidney events based on whether people in the study had insulin resistance or not before treatment

Heart events

They used the combined measure to compare the risk of having a heart event in people who:

- Took finerenone and those who took the placebo
- Had insulin resistance and those who did not have insulin resistance

Kidney events

They used the combined measure to compare the risk of having a kidney event in people who:

- Took finerenone compared with those who took the placebo
- Had insulin resistance and those who did not have insulin resistance

What were the Heart event results from the extra analysis?

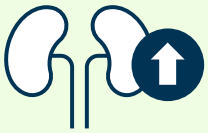
Did insulin resistance increase the risk of a heart event?

After 3.5 years:

Yes. People **with** insulin resistance had **a higher chance** of having heart events than people who **did not have** insulin resistance

Did insulin resistance increase the risk of a kidney event?

After 3.5 years:



No. People **with** insulin resistance had **a similar chance** of having kidney events as people who **did not have** insulin resistance

What heart outcomes did the researchers find in people who took finerenone?

Overall:

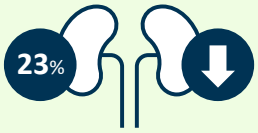
People who took **finerenone had a 14% lower chance of heart events** compared with people who took **placebo**

Insulin resistance did not change how well finerenone worked

People who took finerenone and **had insulin resistance** had a similar chance of heart events as people who took finerenone and **did not have insulin resistance**

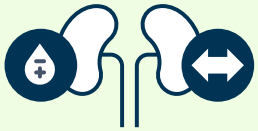
What kidney outcomes did the researchers find in people who took finerenone?

Overall:



People who took **finerenone had a 23% lower chance of kidney events** compared with people who took **placebo**

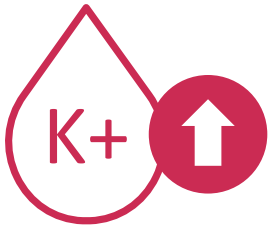
Insulin resistance did not change how well finerenone worked



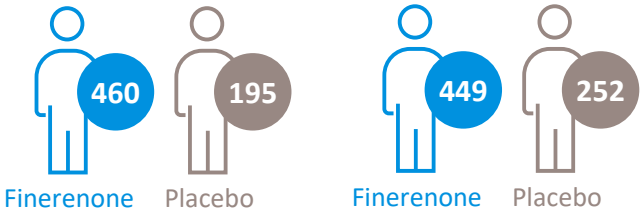
People who took **finerenone and had insulin resistance had a similar chance of kidney events** as people who took finerenone and did not have insulin resistance

What side effects did people in the study have?

- Researchers looked at side effects (health problems) that people had after starting treatment with finerenone or placebo
- The number and types of side effects were recorded in people who took finerenone and in people who took placebo
  - The proportions of people who had side effects were similar in the group who took finerenone and in the group who took the placebo
- A side effect that was more common in people who took finerenone was an increased level of potassium in their blood. This is called hyperkalemia
  - However, the proportion of people who stopped taking finerenone was similar to the proportion of people who stopped taking placebo due to hyperkalemia
- People who took finerenone and had insulin resistance had a similar number and types of side effects as people who took finerenone and did not have insulin resistance



Hyperkalemia



With insulin resistance

Without insulin resistance

What were the main conclusions of this extra analysis using data from the FIDELITY study?

- Insulin resistance increased the chance of having heart events in people with T2D and CKD
  - Insulin resistance did not change the risk of kidney events
- Finerenone worked as well in people who had T2D and CKD whether they had insulin resistance or not before they started treatment
- People who took finerenone who had insulin resistance had similar side effects to people who did not have insulin resistance

Who sponsored this study?

Bayer AG

Where can I find more information?

Study IDs:

- NCT02540993 (FIDELIO-DKD)
- NCT02545049 (FIGARO-DKD)

Website: https://clinicaltrials.gov/

The full citation of the abstract is:

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It was presented at: the American Diabetes Association (ADA) 2023 (June 23-24, 2023, San Diego, CA, USA).

This summary was prepared by Envision Pharma Group. The original authors of the full poster presentation were not involved in preparing this summary.

The full title of this abstract is:

Outcomes with finerenone in people with chronic kidney disease and type 2 diabetes by baseline insulin resistance: a FIDELITY subgroup analysis

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Please note this summary focuses on the scientific abstract.

https://diabetesjournals.org/diabetes/article/72/Supplement_1/829-P/150525/829-P-Outcomes-with-Finerenone-in-People-with-CKD *Diabetes* 2023;72(Supplement_1):829-P. For wider context, some aspects of the associated congress poster have also been included in this plain language summary (Poster 29-9, presented at the American Diabetes Association (ADA) 2023 meeting (June 23–26, 2023, San Diego, CA, USA)

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