A parallel-group treatment, Phase 2, double-blind, three-arm study to assess efficacy and safety of finerenone plus empagliflozin compared with either finerenone or empagliflozin in participants with chronic kidney disease and type 2 diabetes

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This study has been transitioned to CTIS with ID 2023-506981-30-00 check the CTIS register for the current data. Main objective:The primary objective is to demonstrate that combination therapy using finerenone and empagliflozin is superior in...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON53849

Source
ToetsingOnline

Brief title
CONFIDENCE: finerenone and empagliflozin in participants with CKD and T2D

Condition

- Diabetic complications

Synonym
Chronic Kidney Disease and Diabetes type 2

Research involving
Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: Pharmaceutical Company

Intervention

Keyword: CKD, Empagliflozin, Finerenone, T2D

Outcome measures

Primary outcome

Relative change from baseline in UACR at 180 days in combination therapy group versus empagliflozin alone

Relative change from baseline in UACR at 180 days in combination therapy group versus finerenone alone

Secondary outcome

1. Relative change in UACR between end of treatment visit and 30 days after end of treatment visit 2. Relative change in UACR between 30 days after end of treatment visit and baseline 3. Relative change in UACR category (>30%, >40%, >50%) at 180 days 4. Ratio of change from baseline in eGFR at 30 days 5. eGFR decline greater than 30% at 30 days from baseline 6. Ratio of change in eGFR at 180 days and 210 days from day 30 7. Number of participants with of AKI events 8. Total number of AKI events 9. Number of participants with hyperkalemia events (moderate hyperkalemia [5.5 6.0 mmol/L]) 10. Total number of hyperkalemia events (moderate hyperkalemia [5.5 6.0 mmol/L])

Study description

Background summary

Finerenone works by blocking a group of proteins, called mineralocorticoid receptor. An increased stimulation of mineralocorticoid receptor is known to trigger injury and inflammation in the kidney and is therefore thought to play a role in CKD.

Empagliflozin lowers blood sugar levels by increasing the excretion of glucose from the blood into the urine.

In this study, the researchers want to learn how well the combination of finerenone and empagliflozin helps to slow down the worsening of the participants* kidney function compared to either treatment alone. For this, the level of protein in the urine will be measured. They also want to know how safe the combination is compared to either treatment alone.

This is the first parallel-group randomized controlled trial to evaluate the safety, tolerability, and additive efficacy of the combined use of finerenone and empagliflozin using the surrogate endpoint of UACR (urinary albumin-to-creatinine ratio). This study will also investigate, for the first time, simultaneous initiation of finerenone and empagliflozin.
The goal of this study is to show that the combined use of finerenone and empagliflozin is superior to either empagliflozin alone, or finerenone alone in reducing UACR at 180 days.

Study objective

This study has been transitioned to CTIS with ID 2023-506981-30-00 check the CTIS register for the current data.

Main objective:
The primary objective is to demonstrate that combination therapy using finerenone and empagliflozin is superior in reducing UACR than either empagliflozin or finerenone alone.

Secondary objectives:
- To further investigate the efficacy of combination therapy using finerenone and empagliflozin versus either finerenone or empagliflozin alone.
- To evaluate the safety of combination therapy using finerenone and empagliflozin versus either finerenone or empagliflozin alone.

Study design

Phase 2, randomized, controlled, double-blind (participants and investigators), doubledummy, multicenter study in participants with CKD and T2D.

Participants and investigators will be blinded to study intervention allocation ensuring a double-blind design, thus limiting bias.

The study will consist of 2 consecutive parts:
o Part A: participants will be recruited if their eGFR is between 40 and 90 ml/min/1.73 m², and they will be equipped with an ABPM at Visit 2 for a duration of 24 hours. An interactive web response system (IWRS) will allow capping the number of participants as follows:
* 80% with an eGFR between <=75 ml/min/1.73 m²
* 20% with an eGFR between >75 ml/min/1.73 m².
o Part B: participants will be recruited if their eGFR is between 30 and 90 ml/min/1.73 m², and they will not have an ABPM. The IWRS will allow capping the number of participants as follows:
* 80% with an eGFR between <=75 ml/min/1.73 m²
* 20% with an eGFR between >75 ml/min/1.73 m².
o The decision to move from Part A to Part B will be taken by the sponsor and the study*s SC upon feedback from the DMC. The safety analysis from the first 50 participants in Part A, as well as their unblinded review by the independent DMC will be used to confirm the enrollment/recruitment start for Part B. This decision shall be effective immediately or after IRB/IEC and/or local Health Authority approval, where applicable.
o Other inclusion/exclusion criteria or study*s schedule or procedure should not be affected.

Participants will be randomized in a 1:1:1 ratio stratified by eGFR at screening (<60, >=60 mL/min/1.73m²) and UACR (<= 850mg/g, > 850 mg/g), using the baseline median from FIDELIO-DKD study) in one of the 3 parallel groups:
o Finerenone (10 or 20 mg once daily [OD]) and empagliflozin (10 mg OD)
o Finerenone (10 or 20 mg OD) and matching placebo to empagliflozin (OD)
o Empagliflozin (10 mg OD) and matching placebo to finerenone (OD).

Intervention

Depending on the treatment group, the participants will either take:

- the combination of finerenone and empagliflozin,
- finerenone together with a placebo,
- empagliflozin together with a placebo,
once a day as tablets by mouth.

Importantly, the participants will also continue to take their other current

medicine for CKD and T2D.

The participants will be in the study for up to 7.5 months and will take the study treatments for 6 months. During the study, they will visit the study site 7 times.
The study team will:
• collect blood and urine samples
• check the participants* vital signs
• do a physical examination including height and weight
• check the participants* heart health by using an electrocardiogram (ECG)
• monitor the participants* blood pressure
• ask the participants questions about how they are feeling and what adverse events they may be having

Study burden and risks

- 7 visits to the hospital divided over 7.5 months
- 4 x (max.) 19 ml blood is collected = 133 ml in total
- blood pressure measurement at home (24-hour collection)
- pregnancy test (if applicable) (3x)
- ECGs (2x)
- other urine tests for safety and how the medication works (UACR).

CONFIDENCE will be the first controlled clinical trial where finerenone and empagliflozin are simultaneously initiated. As mentioned above (protocol p23), initiation of each single drug can lead to a decrease in BP and eGFR. The additive effect of both drugs on BP and eGFR is not yet known. To monitor the risk of hypotension, all participants will be equipped with an ABPM device 1 hour before the first intake at the study site. The participant will remain 4 to 6 hours at the study site for office BP monitoring and will keep the ABPM for 24 hours. eGFR will be monitored at each study visit with a first assessment 14 days after the initial intake. With regards to risks specific to empagliflozin, participants with risks factors for ketoacidosis or volume depletion will be excluded from the study. Participants will also be monitored to look for signs and symptoms of ketoacidosis. Concomitant therapy with insulin will also be carefully monitored and assessed during the medical review.

Reduction in UACR, a surrogate marker for renal outcomes, is correlated with improved renal and cardiovascular outcomes. Therefore, early and efficient intervention, resulting in slower disease progression and potentially prevention of disease progression, may provide long-term benefits for patients with CKD and T2D. By taking part in this study, participants treated with finerenone and empagliflozin combination could benefit from a more effective treatment to reduce CKD progression together with decreased risk of adverse drug reactions.

Contacts

Public
Bayer

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Scientific
Bayer

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

2a:
1. Participant with a clinical diagnosis of chronic kidney disease (CKD) and the following:
a. In Part A: eGFR 40-90 ml/min/1.73m^2 (with no more than 20% having an eGFR >75 ml/min/1.73m^2) using Chronic Kidney Disease Epidemiology Collaboration (CKD EPI) formula at screening visit and at least one historical value of eGFR <60 mL/min/1.73 m^2 within 3 months or have a registered diagnosis of CKD.
b. In Part B: eGFR 30-90 ml/min/1.73m^2 (with no more than 20% having an eGFR >75 ml/min/1.73m^2) using CKD-EPI formula at screening visit and at least one historical value of eGFR <60 mL/min/1.73 m^2 within 3 months or have a registered diagnostic of CKD.
2b:

c. 100 <=UACR <5000 mg/g at screening visit (mean value from 3 morning void samples) and documentation of albuminuria/proteinuria (quantitative or semi-quantitative measurement) in the participant*s medical records at least 3 months prior to screening
2. Participant with type 2 diabetes (T2D) as defined by the American Diabetes Association (ADA 2021), with glycated hemoglobin (HbA1c) at screening <11%.
3. Participant treated with the clinically maximum tolerated dose, as per investigator judgment, of angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB), but not both, for more than 1 month at screening visit.

Exclusion criteria

1. Participants with type 1 diabetes (T1D).
2. Participant with hepatic insufficiency classified as Child-Pugh C.
3. Participant with blood pressure at Day 1 (Visit 2) visit higher than 160 SBP or 100 DBP or systolic blood pressure lower than 90 mmHg.
4. Participant currently treated with a sodium/glucose cotransporter-2 inhibitor (SGLT2i) or SGLT-1/2i or who received a SGLT2i or SGLT-1/2i which cannot be discontinued at least 8 weeks prior to the screening visit and during study intervention treatment.
5. Participant treated with another mineralocorticoid receptor antagonist (MRA) (e.g., eplerenone, esaxerenone, spironolactone, canrenone), a renin inhibitor, potassium supplements, a potassium sparing diuretic (e.g., amiloride, triamterene), a potassium binder agent, or angiotensin receptor-neprilysin inhibitor (ARNI) which cannot be discontinued at least 8 weeks prior to the screening visit and during study intervention treatment.
6. Participants currently treated or who were treated with Finerenone (Kerendia©) within 8 weeks prior to the screening visit.
7. Participant with serum/plasma potassium (K+) above 4.8 mmol/L at screening.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-07-2022
Enrollment:	35
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Finerenone
Generic name:	BAY 94-8862
Product type:	Medicine
Brand name:	Jardiance
Generic name:	Empagliflozin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	16-03-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-06-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-07-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-07-2022

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-12-2022
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	17-01-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	05-07-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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Approved WMO Date:	28-08-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	02-01-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-01-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-02-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-506981-30-00
EudraCT	EUCTR2021-003037-11-NL
CCMO	NL80487.018.22