FULL PRESCRIBING INFORMATION

1. NAME OF THE MEDICINAL PRODUCT

Kerendia 10 mg

Kerendia 20 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Kerendia 10 mg film-coated tablets

Each film-coated tablet contains 10 mg of finerenone.

Kerendia 20 mg film-coated tablets

Each film-coated tablet contains 20 mg of finerenone.

For the full list of excipients, see section 12.

3. PHARMACEUTICAL FORM

Kerendia 10 mg film-coated tablets

Pink Film-coated tablet, oval oblong, diameter of 10 mm and radius of curvature of 3.4 mm, Marked with “10” on Top side, and “FI” on the Bottom side

Kerendia 20 mg film-coated tablets

Pale Yellow Film-coated tablet, oval oblong, diameter of 10 mm and radius of curvature of 3.4 mm, Marked with “20” on Top side, and “FI” on the Bottom side.

4. THERAPEUTIC INDICATIONS

Kerendia is indicated to reduce the risk of sustained eGFR decline, end-stage kidney disease, cardiovascular death, non-fatal myocardial infarction, and hospitalization for heart failure in adult patients with chronic kidney disease (CKD) associated with type 2 diabetes (T2D).

5. DOSAGE AND ADMINISTRATION

5.1 Prior to Initiation of Kerendia

Measure serum potassium levels and estimated glomerular filtration rate (eGFR) before initiation. Do not initiate treatment if serum potassium is > 5.0 mEq/L *[see Warnings and Precautions (7.1)]*.

5.2 Recommended Starting Dosage

The recommended starting dose of Kerendia is based on eGFR and is presented in Table 1.

Table 1: Recommended Starting Dosage

eGFR (mL/min/1.73m^2)	Starting Dose
≥ 60	20 mg once daily
≥ 25 to < 60	10 mg once daily
< 25	Not Recommended

For patients who are unable to swallow whole tablets, Kerendia may be crushed and mixed with water or soft foods such as applesauce immediately prior to use and administered orally *[see Clinical Pharmacology (13.3)]*.

5.3 Monitoring and Dose Adjustment

The target daily dose of Kerendia is 20 mg.

Measure serum potassium 4 weeks after initiating treatment and adjust dose (see Table 2); if serum potassium levels are > 4.8 to 5.0 mEq/L, initiation of Kerendia treatment may be considered with additional serum potassium monitoring within the first 4 weeks based on clinical judgement and serum potassium levels *[see Warnings and Precautions (7.1)]*. Measureserum potassium 4 weeks after a dose adjustment and periodically throughout treatment, and adjust the dose as needed (see Table 2) *[see Warnings and Precautions (7.1) and Drug Interactions (9.1)]*.

Table 2: Dose Adjustment Based on Current Serum Potassium Concentration and Current Dose

		Current Kerendia Dose	
		10 mg once daily	**20 mg once daily**
Current Serum Potassium (mEq/L)	**≤ 4.8**	Increase the dose to 20 mg once daily.*	Maintain 20 mg once daily.
	> 4.8 – 5.5	Maintain 10 mg once daily.	Maintain 20 mg once daily.
	> 5.5	Withhold Kerendia. Consider restarting at 10 mg once daily when serum potassium ≤ 5.0 mEq/L.	Withhold Kerendia. Restart at 10 mg once daily when serum potassium ≤ 5.0 mEq/L.

* If eGFR has decreased by more than 30% compared to previous measurement, maintain 10 mg dose.

5.4 Missed Doses

Direct a patient to take a missed dose as soon as possible after it is noticed, but only on the same day. If this is not possible, the patient should skip the dose and continue with the next dose as prescribed.

6 CONTRAINDICATIONS

Kerendia is contraindicated in patients:

- With hypersensitivity to the active substance or to any of the excipients listed in section 12.
- Who are receiving concomitant treatment with strong CYP3A4 inhibitors *[see Drug Interactions (9.1)]*.
- With adrenal insufficiency.

7 WARNINGS AND PRECAUTIONS

7.1 Hyperkalemia

Kerendia can cause hyperkalemia *[(see Adverse Reactions (8.1)]*.

The risk for developing hyperkalemia increases with decreasing kidney function and is greater in patients with higher baseline potassium levels or other risk factors for hyperkalemia. Measure serum potassium and eGFR in all patients before initiation of treatment with Kerendia and dose accordingly *[see Dosage and Administration (5.1)]*. Do not initiate Kerendia if serum potassium is > 5.0 mEq/L.

Measure serum potassium periodically during treatment with Kerendia and adjust dose accordingly *[see Dosage and Administration (5.3)]*. More frequent monitoring may be necessary for patients at risk for hyperkalemia, including those on concomitant medications that impair potassium excretion or increase serum potassium *[see Drug Interactions (9.1), 9.2)]*.

7.2 Worsening of Renal Function in Patients with Heart Failure

Kerendia can cause worsening of renal function in patients with heart failure. Rarely, severe events associated with worsening renal function, including events requiring hospitalization, have been observed.

Measure eGFR in all patients before initiation of treatment or with dose titration of Kerendia and dose accordingly *[see Dosage and Administration (*5.1,5.3*)]*. Initiation of Kerendia in patients with heart failure and an eGFR <25 mL/min/1.73m2 is not recommended.

Measure eGFR periodically during maintenance treatment with Kerendia in patients with heart failure. Consider delaying up-titration or interrupting treatment with Kerendia in patients who develop clinically significant worsening of renal function.

8 ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in the labeling:

- Hyperkalemia *[see Warnings and Precautions (7.1)]*

8.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of Kerendia was evaluated in 2 randomized, double-blind, placebo-controlled, multicenter pivotal phase 3 studies FIDELIO-DKD and FIGARO-DKD, in which a total of 6510 patients were treated with 10 or 20 mg once daily over a mean duration of 2.2 years and 2.9 years, respectively.

Overall, serious adverse events occurred in 32% of patients receiving Kerendia and in 34% of patients receiving placebo in the FIDELIO-DKD study; the finding were similar in the FIGARO-DKD study. Permanent discontinuations due to adverse events occurred in a similar proportion of patients in the two studies (6-7% of patients receiving Kerendia and in 5-6% of patients receiving placebo).

The most frequently reported (≥ 10%) adverse reaction in both studies was hyperkalemia *[see Warnings and Precautions (7.1)]*. Hospitalization due to hyperkalemia for the Kerendia group was 0.9% vs 0.2% in the placebo group across both studies. Hyperkalemia led to permanent discontinuation of treatment in 1.7% receiving Kerendia versus 0.6% of patients receiving placebo across both studies.

Table 3 shows adverse reactions that occurred more commonly on Kerendia than on placebo, and in at least 1% of patients treated with Kerendia.

Table 3: Adverse reactions reported in ≥ 1% of patients on Kerendia and more frequently than placebo (Pooled data from FIDELIO-DKD and FIGARO-DKD)

Adverse reactions	Kerendia N = 6510	Placebo N = 6489

	n (%)	n (%)
Hyperkalemia	912 (14.0)	448 (6.9)
Hypotension	302 (4.6)	194 (3.0)
Hyponatremia	82 (1.3)	47 (0.7)

Laboratory Test

Initiation of Kerendia may cause an initial small increase in blood creatinine levels (mean change <0.1 mg/dL) and a small decrease in eGFR (mean change 2-3 ml/min) that occurs within the first 4 weeks of starting therapy, and then stabilizes. These changes were reversible after treatment discontinuation.

Initiation of Kerendia may also cause a small increase in serum uric acid. This increase appears to attenuate over time.

8.2 Postmarketing Experience

The following additional adverse reactions have been reported in postmarketing experience with finerenone. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency reliably or to establish a causal relationship to drug exposure:

Hypersensitivity: Angioedema, Rash and Urticaria

9 DRUG INTERACTIONS

9.1 CYP3A4 Inhibitors and Inducers

Strong CYP3A4 Inhibitors

Kerendia is a CYP3A4 substrate. Concomitant use with a strong CYP3A4 inhibitor increases finerenone exposure *[see Clinical Pharmacology (13.3)]*, which may increase the risk of Kerendia adverse reactions. Concomitant use of Kerendia with strong CYP3A4 inhibitors is contraindicated *[see Contraindications (6)]*. Avoid concomitant intake of grapefruit or grapefruit juice.

Moderate and Weak CYP3A4 Inhibitors

Kerendia is a CYP3A4 substrate. Concomitant use with a moderate or weak CYP3A4 inhibitor increases finerenone exposure *[see Clinical Pharmacology (13.3)]*, which may increase the risk of Kerendia adverse reactions. Monitor serum potassium during drug initiation or dosage adjustment of either Kerendia or the moderate or weak CYP3A4 inhibitor, and adjust Kerendia dosage as appropriate *[see Dosing and Administration (5.3) and Drug Interaction (9.2)]*.

Strong and Moderate CYP3A4 Inducers

Kerendia is a CYP3A4 substrate. Concomitant use of Kerendia with a strong or moderate CYP3A4 inducer decreases finerenone exposure *[see Clinical Pharmacology (13.3)],* which may reduce the efficacy of Kerendia. Avoid concomitant use of Kerendia with strong or moderate CYP3A4 inducers.

9.2 Drugs That Affect Serum Potassium

More frequent serum potassium monitoring is warranted in patients receiving concomitant therapy with drugs or supplements that increase serum potassium. *[see Dosage and Administration (5.3) and Warnings and Precautions (7.1)]*.

10 USE IN SPECIFIC POPULATIONS

10.1 Pregnancy

Risk Summary

There are no available data on Kerendia use in pregnancy to evaluate for a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Animal studies have shown developmental toxicity at exposures about 4 times those expected in humans. *(see Data)*. The clinical significance of these findings is unclear.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Animal Data

In the embryo-fetal toxicity study in rats, finerenone resulted in reduced placental weights and signs of fetal toxicity, including reduced fetal weights and retarded ossification at the maternal toxic dose of 10 mg/kg/day corresponding to an $AUC_{unbound}$ of 19 times that in humans. At 30 mg/kg/day, the incidence of visceral and skeletal variations was increased (slight edema, shortened umbilical cord, slightly enlarged fontanelle) and one fetus showed complex malformations including a rare malformation (double aortic arch) at an $AUC_{unbound}$ of about 25 times that in humans. The doses free of any findings (low dose in rats, high dose in rabbits) provide safety margins of 10 to 13 times for the $AUC_{unbound}$ expected in humans.

When rats were exposed during pregnancy and lactation in the pre- and postnatal developmental toxicity study, increased pup mortality and other adverse effects (lower pup weight, delayed pinna unfolding) were observed at about 4 times the $AUC_{unbound}$ expected in humans. In addition, the offspring showed slightly increased locomotor activity, but no other neurobehavioral changes starting at about 4 times the $AUC_{unbound}$ expected in humans. The dose free of findings provides a safety margin of about 2 times for the $AUC_{unbound}$ expected in humans.

10.2 Lactation

Risk Summary

There are no data on the presence of finerenone or its metabolite in human milk, the effects on the breastfed infant or the effects of the drug on milk production. In a pre- and postnatal developmental toxicity study in rats, increased pup mortality and lower pup weight were observed at about 4 times the $AUC_{unbound}$ expected in humans. These findings suggest that finerenone is present in rat milk *[see Use in Specific Populations (10.1) and Data].* When a drug is present in animal milk, it is likely that the drug will be present in human milk. Because of the potential risk to breastfed infants from exposure to KERENDIA, avoid breastfeeding during treatment and for 1 day after treatment.

10.4 Pediatric Use

The safety and efficacy of Kerendia have not been established in children and adolescents below 18 years of age.

10.5 Geriatric Use

Of the 6510 patients who received Kerendia in the FIDELIO-DKD and FIGARO-DKD studies , 55%% of patients were 65 years and older, and 14% were 75 years and older. No overall differences in safety or efficacy were observed between these patients and younger patients. No dose adjustment is required.

10.6 Hepatic Impairment

Avoid use of Kerendia in patients with severe hepatic impairment (Child Pugh C).

No dosage adjustment is recommended in patients with mild or moderate hepatic impairment (Child Pugh A or B).

Consider additional serum potassium monitoring in patients with moderate hepatic impairment (Child Pugh B) *[see Dosing and Administration (5.3) and Clinical Pharmacology (13.3)]*.

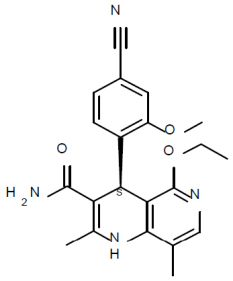
11 OVERDOSAGE

In the event of suspected overdose, immediately interrupt Kerendia treatment. The most likely manifestation of overdose is hyperkalemia. If hyperkalemia develops, standard treatment should be initiated.

Finerenone is unlikely to be efficiently removed by hemodialysis given its fraction bound to plasma proteins of about 90%.

12 DESCRIPTION

Kerendia contains finerenone, a nonsteroidal mineralocorticoid receptor antagonist. Finerenone's chemical name is (*4S*)-4-(4-cyano-2- methoxyphenyl)-5-ethoxy-2,8-dimethyl-1,4-dihydro-1,6-naphthyridine-3-carboxamide. The molecular formula is $C_{21}H_{22}N_4O_3$ and the molecular weight is 378.43 g/mol. The structural formula is:



Finerenone is a white to yellow crystalline powder. It is practically insoluble in water; and sparingly soluble in 0.1 M HCl, ethanol, and acetone.

Each Kerendia tablet contains 10 mg or 20 mg of finerenone. The inactive ingredients of Kerendia are cellulose microcrystalline, lactose monohydrate, croscarmellose sodium, hypromellose, magnesium stearate and sodium lauryl sulfate. The film coating contains hypromellose, titanium dioxide and talc, in addition to ferric oxide red (10 mg strength tablets) or ferric oxide yellow (20 mg strength tablets).

13 CLINICAL PHARMACOLOGY

13.1 Mechanism of Action

Finerenone is a nonsteroidal, selective antagonist of the mineralocorticoid receptor (MR), which is activated by aldosterone and cortisol and regulates gene transcription. Finerenone blocks MR mediated sodium reabsorption and MR overactivation in both epithelial (e.g., kidney) and nonepithelial (e.g., heart, and blood vessels) tissues. MR overactivation is thought to contribute to fibrosis and inflammation. Finerenone has a high potency and selectivity for the MR and has no relevant affinity for androgen, progesterone, estrogen, and glucocorticoid receptors.

13.2 Pharmacodynamics

In FIDELIO-DKD and FIGARO-DKD, randomized, double-blind, placebo-controlled, multicenter studies in adult patients with chronic kidney disease associated with type 2 diabetes, the placebo-corrected relative reduction in urinary albumin-to-creatinine ratio (UACR) in patients randomized to finerenone was 31% (95% CI 29-34%) and 32% (95% CI 30-35%) respectively at Month 4 and remained stable for the duration of the trial.

In ARTS DN, a randomized, double-blind, placebo-controlled, multicenter phase IIb dose finding study in adults with CKD and T2DM, the placebo-corrected relative reduction in UACR at Day 90 was 25% and 38% in patients treated with finerenone 10 mg and 20 mg once daily, respectively.

In patients treated with Kerendia, the mean systolic blood pressure decreased by 3 mmHg and the mean diastolic blood pressure decreased by 1-2 mmHg at month 1, remaining stable thereafter.

Cardiac Electrophysiology

At a dose 4 times the maximum approved recommended dose, finerenone does not prolong the QT interval to any clinically relevant extent.

13.3 Pharmacokinetics

Finerenone exposure increased proportionally over a dose range of 1.25 to 80 mg (0.06 to 4 times the maximum approved recommended dosage). Steady state of finerenone was achieved after 2 days of dosing. The estimated steady-state geometric mean $C_{max,md}$ was 166 µg/L and steady-state geometric mean $AUC_{\tau,md}$ was 718 µg.h/L following administration of finerenone 20 mg to patients.

Absorption

Finerenone is completely absorbed after oral administration but undergoes metabolism resulting in absolute bioavailability of 44%. Finerenone C_{max} was achieved between 0.5 and 1.25 hours after dosing.

Effect of Food

There was no clinically significant effect on finerenone AUC following administration with high fat, high calorie food.

Distribution

The volume of distribution at steady-state (Vss) of finerenone is 52.6 L. Plasma protein binding of finerenone is 92%, primarily to serum albumin, in vitro.

Elimination

The terminal half-life of finerenone is about 2 to 3 hours, and the systemic blood clearance is about 25 L/h.

Metabolism

Finerenone is primarily metabolized by CYP3A4 (90%) and to a lesser extent by CYP2C8 (10%) to inactive metabolites.

Excretion

About 80% of the administered dose is excreted in urine (<1% as unchanged) and approximately 20% in feces (< 0.2% as unchanged).

Specific Populations

There are no clinically significant effects of age (18 to 79 years), sex, race/ethnicity (White, Asian, Black, and Hispanic), or weight (58 to 121 kg) on the pharmacokinetics of finerenone.

Renal Impairment

There were no clinically relevant differences in finerenone AUC or C_{max} values in patients with eGFR 15 to < 90 mL/min/1.73m^2 compared to eGFR ≥ 90 mL/min/1.73 m^2. For dosing recommendations based on eGFR and serum potassium levels *see Dosage and Administration (5)*.

Hepatic Impairment

There was no clinically significant effect on finerenone exposure in cirrhotic patients with mild hepatic impairment (Child Pugh A).

Finerenone mean AUC was increased by 38% and C_{max} was unchanged in cirrhotic patients with moderate hepatic impairment (Child Pugh B) compared to healthy control subjects.

The effect of severe hepatic impairment (Child Pugh C) on finerenone exposure was not studied.

Drug Interaction Studies

Clinical Studies and Model-Informed Approaches

Strong CYP3A Inhibitors: Concomitant use of itraconazole (strong CYP3A4 inhibitor) was predicted to increase finerenone AUC by >400%.

Moderate CYP3A Inhibitors: Concomitant use of erythromycin (moderate CYP3A4 inhibitor) increased finerenone mean AUC and C_{max} by 248% and 88%, respectively. Concomitant use of verapamil (moderate CYP3A4 inhibitor) increased finerenone mean AUC and C_{max} by 170% and 122%, respectively.

Weak CYP3A Inhibitors: Concomitant use of amiodarone (weak CYP3A4 inhibitor) increased finerenone AUC by 21%.

Strong or Moderate CYP3A Inducers: Concomitant use of efavirenz (moderate CYP3A4 inducer) and rifampicin (strong CYP3A4 inducer) was predicted to decrease finerenone AUC by 80% and 90%, respectively.

Other Drugs: No clinically significant differences in the pharmacokinetics of the following drugs were observed or predicted when used concomitantly with finerenone: S-warfarin (CYP2C9 substrate), digoxin (P-gp substrate), and rosuvastatin (BCRP and OATP substrate) There was no clinically significant difference in finerenone pharmacokinetics when used concomitantly with gemfibrozil (strong CYP2C8 inhibitor)

14 NONCLINICAL TOXICOLOGY

14.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Finerenone was non-genotoxic in an in vitro bacterial reverse mutation (Ames) assay, the in vitro chromosomal aberration assay in cultured Chinese hamster V79 cells, or the in vivo micronucleus assay in mice.

In 2-year carcinogenicity studies, finerenone did not show a statistically significant increase in tumor response in Wistar rats or in CD1 mice. In male mice, Leydig cell adenoma was numerically increased at a dose representing 26 times the $AUC_{unbound}$ in humans and is not considered clinically relevant. Finerenone did not impair fertility in male rats but impaired fertility in female rats at 20 times AUC to the maximum human exposure.

15 CLINICAL STUDIES

FIDELIO-DKD (NCT: 02540993) and FIGARO-DKD (NCT: 02545049) studies were randomized, double-blind, placebo-controlled, multicenter studies in adult patients with chronic kidney disease (CKD) associated with type 2 diabetes (T2DM). In FIDELIO-DKD, patients needed to either have an UACR of 30 to < 300 mg/g, eGFR 25 to < 60 mL/min/1.73 m^2 and diabetic retinopathy, or an UACR of ≥ 300 mg/g and an eGFR of 25 to < 75 mL/min/1.73 m^2 to qualify for enrollment. In FIGARO-DKD, patients needed to have an UACR of 30 mg/g to < 300 mg/g and an eGFR of 25 to 90 mL/min/1.73m^2, or an UACR ≥ 300 mg/g and an eGFR ≥ 60 mL/min/1.73m^2.

Both trials excluded patients with known significant non-diabetic kidney disease. All patients were to have a serum potassium ≤ 4.8 mEq/L at screening and be receiving standard of care background therapy, including a maximum tolerated labeled dose of an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB). Patients with a clinical diagnosis of chronic heart failure with reduced ejection fraction and persistent symptoms (New York Heart Association class II to IV) were excluded. The starting dose of Kerendia was based on screening eGFR (10 mg once daily in patients with an eGFR of 25 to < 60 mL/min/1.73 m^2 and 20 mg once daily in patients with an eGFR ≥ 60 mL/min/1.73 m^2). The dose of Kerendia could be titrated during the study, with a target dose of 20 mg daily.

The primary objective of the FIDELIO-DKD study was to determine whether Kerendia reduced the incidence of a sustained decline in eGFR of ≥ 40%, kidney failure (defined as chronic dialysis, kidney transplantation, or a sustained decrease in eGFR to < 15 mL/min/1.73 m^2), or renal death. The secondary outcome was a composite of time to first occurrence of CV death, non-fatal MI, non-fatal stroke or hospitalization for heart failure. The primary objective of the FIGARO-DKD study was to determine whether Kerendia reduced the time to first occurrence of CV death, non-fatal MI, non-fatal stroke or hospitalization for heart failure. The secondary outcome was a composite of time to kidney failure, a sustained decline in eGFR of 40% or more compared to baseline over at least 4 weeks, or renal death.

In FIDELIO-DKD, a total of 5674 patients were randomized to receive Kerendia (N=2833) or placebo (N=2841) and were followed for a median of 2.6 years. The mean age of the study population was 66 years, and 70% of patients were male. This global trial population was 63% White, 25% Asian, and 5% Black. At baseline, the mean eGFR was 44

mL/min/1.73m^2, with 55% of patients having an eGFR < 45 mL/min/1.73m^2. Median urine albumin-to-creatinine ratio (UACR) was 852 mg/g, mean glycated hemoglobin A1c (HbA1c) was 7.7%, and the mean blood pressure was 138/76 mmHg. Approximately 46% of patients had a history of atherosclerotic cardiovascular disease and 8% had a history of heart failure. At baseline, 99.8% of patients were treated with an ACEi or ARB. Approximately 97% were on an antidiabetic agent (insulin [64.1%], biguanides [44%], glucagon-like peptide-1 [GLP-1] receptor agonists [7%], sodium-glucose cotransporter 2 [SGLT2] inhibitors [5%]), 74% were on a statin, and 57% were on an antiplatelet agent.

In FIGARO-DKD, a total of 7352 patients were randomized to receive Kerendia (N=3686) or placebo (N=3666) and were followed for 3.4 years. As compared to FIDELIO-DKD, baseline eGFR was higher in FIGARO-DKD (mean eGFR 68, with 62% of patients having an eGFR ≥ 60 mL/min/1.73 m^2) and median UACR was lower (308 mg/g). Otherwise, baseline patient characteristics and background therapies were similar in the two trials.

In FIDELIO-DKD, Kerendia reduced the incidence of the primary composite endpoint of a sustained decline in eGFR of ≥ 40%, kidney failure, or renal death (HR 0.82, 95% CI 0.73-0.93, p=0.001) as shown in Table 4 and Figure 1. The treatment effect reflected a reduction in a sustained decline in eGFR of ≥ 40% and progression to kidney failure. There were few renal deaths during the trial. Kerendia also reduced the incidence of the secondary composite endpoint of cardiovascular (CV) death, non-fatal myocardial infarction (MI), non-fatal stroke or hospitalization for heart failure (HR 0.86, 95% CI 0.75-0.99, p=0.034) as shown in Table 4 and Figure 3. The treatment effect reflected a reduction in CV death, non-fatal MI, and hospitalization for heart failure. The treatment effect on the primary and secondary composite endpoints was generally consistent across subgroups.

In FIGARO-DKD, Kerendia reduced the incidence of the primary composite endpoint of CV death, non-fatal MI, non-fatal stroke or hospitalization for heart failure (HR 0.87, 95% CI 0.76-0.98, p = 0.026) as shown in Table 4 and Figure 4. The treatment effect was mainly driven by an effect on hospitalization for heart failure, though CV death also contributed to the treatment effect. The treatment effect on the primary composite endpoint was generally consistent across subgroups, including patients with and without pre-existing cardiovascular disease. The findings for the renal composite endpoint are shown in Table 4 and Figure 2.

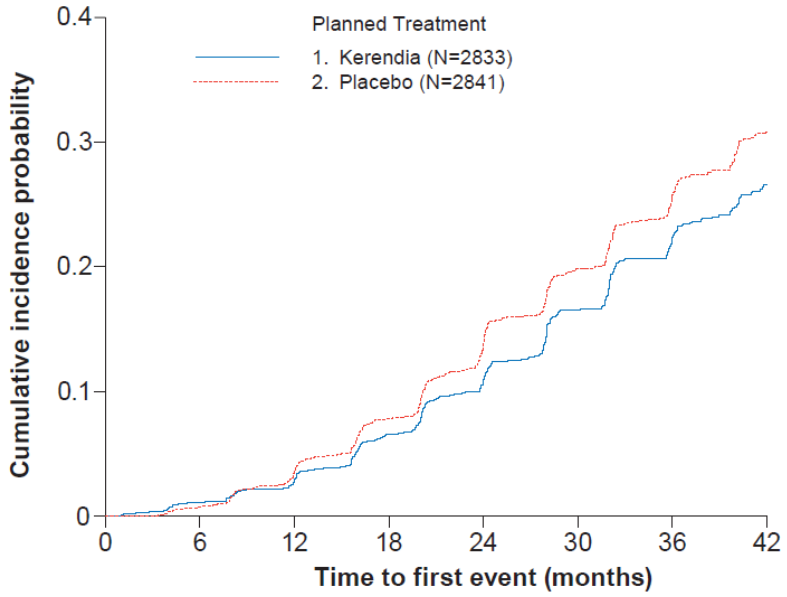
Table 4: Analysis of the Primary and Secondary Time-to-Event Endpoints (and their Individual Components) in Phase 3 Studies FIDELIO-DKD and FIGARO-DKD

	FIDELIO-DKD				FIGARO-DKD			
	Kerendia N=2833	Placebo N=2841	Treatment Effect Kerendia / Placebo		Kerendia N=3686	Placebo N=3666	Treatment Effect Kerendia / Placebo	
Time-to-event Endpoints:	Event Rate (100 pt-yr)	Event Rate (100 pt-yr)	Hazard Ratio (95% CI)	p-value	Event Rate (100 pt-yr)	Event Rate (100 pt-yr)	Hazard Ratio (95% CI)	p-value
Composite of kidney failure, sustained eGFR decline ≥40% or renal death	7.6	9.1	0.82 [0.73; 0.93]	0.001	3.2	3.6	0.87 [0.76; 1.01]	-
Kidney failure	3.0	3.4	0.87 [0.72; 1.05]	-	0.4	0.5	0.72 [0.49;1.05]	-
Sustained eGFR decline ≥40%	7.2	8.7	0.81 [0.72; 0.92]	-	3.1	3.5	0.87 [0.75;>1.00]	-
Renal death	-	-	-	-	-	-	-	-
Composite of CV death, non-fatal MI, non-fatal stroke or hospitalization for heart failure	5.1	5.9	0.86 [0.75; 0.99]	0.034	3.9	4.5	0.87 [0.76; 0.98]	0.026
CV death	1.7	2.0	0.86 [0.68;1.08]	-	1.6	1.8	0.90 [0.73; 1.08]	-
Non-fatal MI	0.9	1.2	0.80 [0.58;1.09]	-	0.9	0.8	0.99 [0.76; 1.32]	-
Non-fatal stroke	1.2	1.2	1.03 [0.76;1.38]	-	0.9	0.9	0.97 [0.74; 1.26]	-
Hospitalization for heart failure	1.9	2.2	0.86 [0.68;1.08]	-	1.0	1.4	0.71 [0.56; 0.90]	-

p-value: two-sided p-value from stratified logrank test
CI = confidence interval, CV = cardiovascular, eGFR = estimated glomerular filtration rate, MI = myocardial infarction, N = number of subjects, n = number of subjects with event, pt-yr = patient year.

NOTE: Time to first event was analyzed in a Cox proportional hazards model. For patients with multiple events, only the first event contributed to the composite endpoint. Sums of the numbers of first events for the single components do not add up to the numbers of events in the composite endpoint

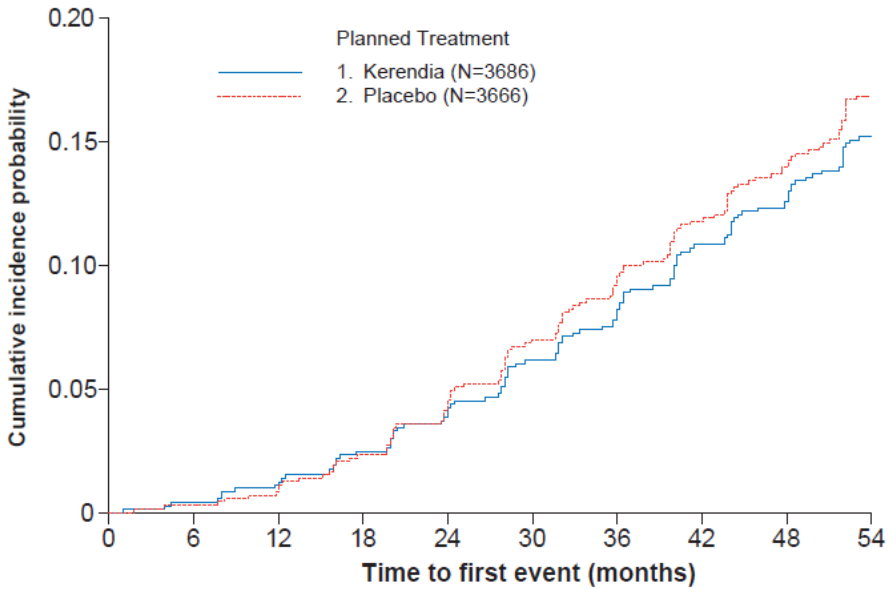
Figure 1: Time to first occurrence of kidney failure, sustained decline in eGFR ≥40% from baseline, or renal death in the FIDELIO-DKD study



No. of patients at risk

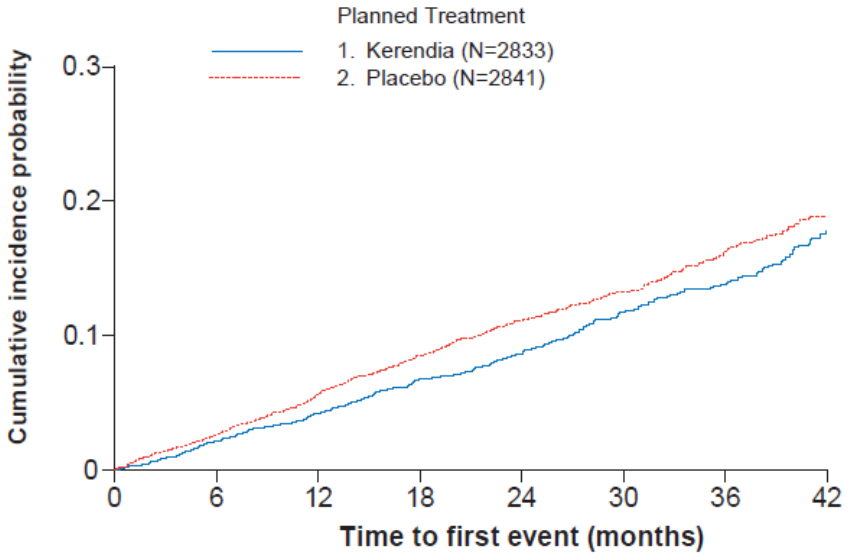
Kerendia	2833	2705	2607	2397	1808	1274	787	441
Placebo	2841	2724	2586	2379	1758	1248	792	453

Figure 2: Time to first occurrence of kidney failure, sustained decline in eGFR ≥ 40% from baseline, or renal death in the FIGARO-DKD study



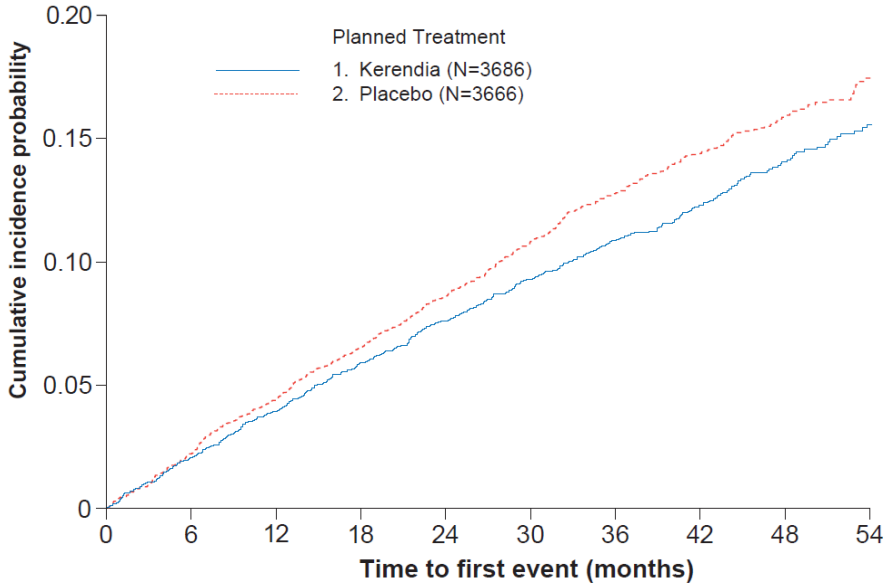
No. of patients at risk										
Kerendia	3686	3550	3445	3301	3131	2540	1940	1481	908	480
Placebo	3666	3546	3436	3282	3096	2507	1933	1443	907	485

Figure 3: Time to first occurrence of CV death, non-fatal myocardial infarction, non-fatal stroke or hospitalization for heart failure in the FIDELIO-DKD study



No. of patients at risk								
Kerendia	2833	2760	2688	2582	2017	1488	984	537
Placebo	2841	2753	2653	2549	1969	1475	951	536

Figure 4: Time to first occurrence of CV death, non-fatal myocardial infarction, non-fatal stroke or hospitalization for heart failure in the FIGARO-DKD study



No. of patients at risk

Kerendia	3686	3600	3517	3427	3320	2781	2184	1712	1093	598
Placebo	3666	3577	3479	3389	3267	2730	2125	1657	1076	585

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Kerendia is available as a film-coated tablet in two strengths. The 10 mg is a pink oblong tablet with “FI” on one side of tablet and “10” on the other side of tablet. The 20 mg tablet is a yellow oblong tablet with “FI” on one side of tablet and “20” on the other side of tablet. Kerendia 10 mg and 20 mg are available in blister stripe of 14, 28 or 98 film-coated tablets or perforated unit dose blisters in cartons of 10 × 1 or 100 × 1 film-coated tablets

Not all pack sizes are marketed.

16.2 Storage and Handling

This medicinal product does not require any special storage conditions.

17. Marketing Authorisation Holder
Bayer Israel Ltd. 36 Hacharash St., Hod Hasharon 45240

18. Manufacturer
Bayer AG 51368 Leverkusen Germany

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