FIND-CKD

Efficacy of finerenone in non-diabetic CKD: Design of the FIND-CKD trial

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Disclosures
Professor Heerspink has received the following:

HJLH has received funding/honoraria and consulting fees to his institution for steering committee membership and/or advisory board participation from AstraZeneca, AbbVie, Janssen, Gilead, Bayer, Chinook, CSL Pharma, and Travere Pharmaceuticals; consulting fees from Boehringer Ingelheim and Novo Nordisk; honoraria for lectures from AstraZeneca; and has participated in advisory boards for Mitsubishi Tanabe and Mundipharma.

His institutions have received research grants for clinical trials from AstraZeneca, AbbVie, Boehringer Ingelheim, Janssen, and Novo Nordisk.

RA reports personal fees and non-financial support from Bayer Healthcare Pharmaceuticals Inc. during the conduct of the study; he also reports personal fees and non-financial support from Akebia Therapeutics, Janssen, Relypsa, Vifor Pharma, Boehringer Ingelheim, Sanofi, Eli Lilly, AstraZeneca, and Fresenius; he has received personal fees from Ironwood Pharmaceuticals, Merck & Co., Lexicon, and Reata, and non-financial support from Otsuka America Pharmaceutical, Opko Pharmaceuticals, and E. R. Squibb & Sons; he is a member of data safety monitoring committees for Amgen, AstraZeneca, and Celgene; a member of steering committees of randomized trials for Akebia Therapeutics, Bayer, Janssen, and Relypsa; a member of adjudication committees for AbbVie, Bayer, Boehringer Ingelheim, and Janssen; he has served as Associate Editor of the *American Journal of Nephrology* and *Nephrology Dialysis and Transplantation* and has been an author for UpToDate; and he has received research grants from the U.S. Veterans Administration and the National Institutes of Health. **GLB** reports research funding, paid to the University of Chicago Medicine from Bayer, during the conduct of the study; he also reports research funding, paid to the University of Chicago Medicine, from Novo Nordisk and Vascular Dynamics; he has acted as a consultant for and received personal fees from Merck, Relypsa, and Alnylam; he is an Editor of the *American Journal of Nephrology*, *Nephrology*, and *Hypertension*, and Section Editor of UpToDate; and he is an Associate Editor of *Diabetes Care* and *Hypertension Research*. **DZIC** has received honoraria from Boehringer Ingelheim-Lilly, Merck, AstraZeneca, Sanofi, Mitsubishi Tanabe, AbbVie, Janssen, Bayer, Prometic, BMS, Maze, CSL-Behring, and Novo Nordisk, and has received operational funding for clinical trials from Boehringer Ingelheim-Lilly, Merck, Janssen, Sanofi, AstraZeneca, and Novo Nordisk. **CSPL** reports research support from Bayer and Roche Diagnostics and that she has served as consultant or on the advisory board/steering committee/executive committee for Actelion, Amgen, AnaCardio AB, Applied Therapeutics, AstraZeneca, Bayer, Boehringer Ingelheim, Boston Scientific, Cytokinetics, Darma Inc., EchoNous Inc, Impulse Dynamics, Ionis Pharmaceutical, Janssen Research & Development LLC, Medscape/WebMD Global LLC, Merck, Novartis, Novo Nordisk, ProSciento Inc, Radcliffe Group Ltd., Roche Diagnostics, Sanofi, and Us2.ai; and that she serves as co-founder & non-executive director of Us2.ai. **BLN** reports personal fees from AstraZeneca, Bayer, and Janssen for advisory boards, steering committee roles, and travel support, with all honoraria paid to his institution. **KT** reports personal fees from AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, Gilead, Goldfinch Bio, Novo Nordisk, and Travere. **CW** reports honoraria from Akebia, AstraZeneca, Bayer, Boehringer-Ingelheim, Eli-Lilly, FMC, GILEAD, GSK, MSD, and Vifor. **MB**, **SD**, and **SS** are employees of Bayer. **PV** reports [TBC]. **VP** reports [TBC]

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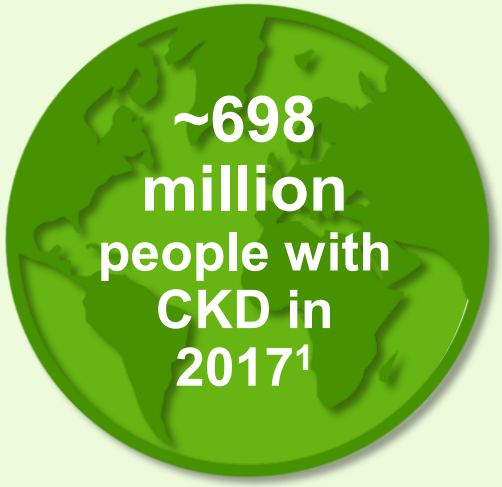
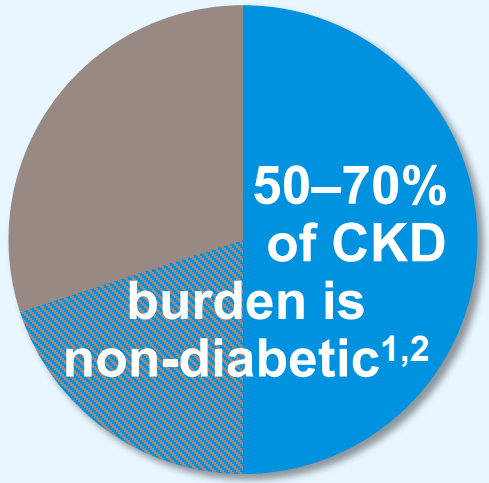
Non-diabetic CKD has a high global disease burden

CKD is a major global health problem, affecting ~9% of the world's population[1]



A substantial proportion of CKD cases have non-diabetic etiologies[1,2]

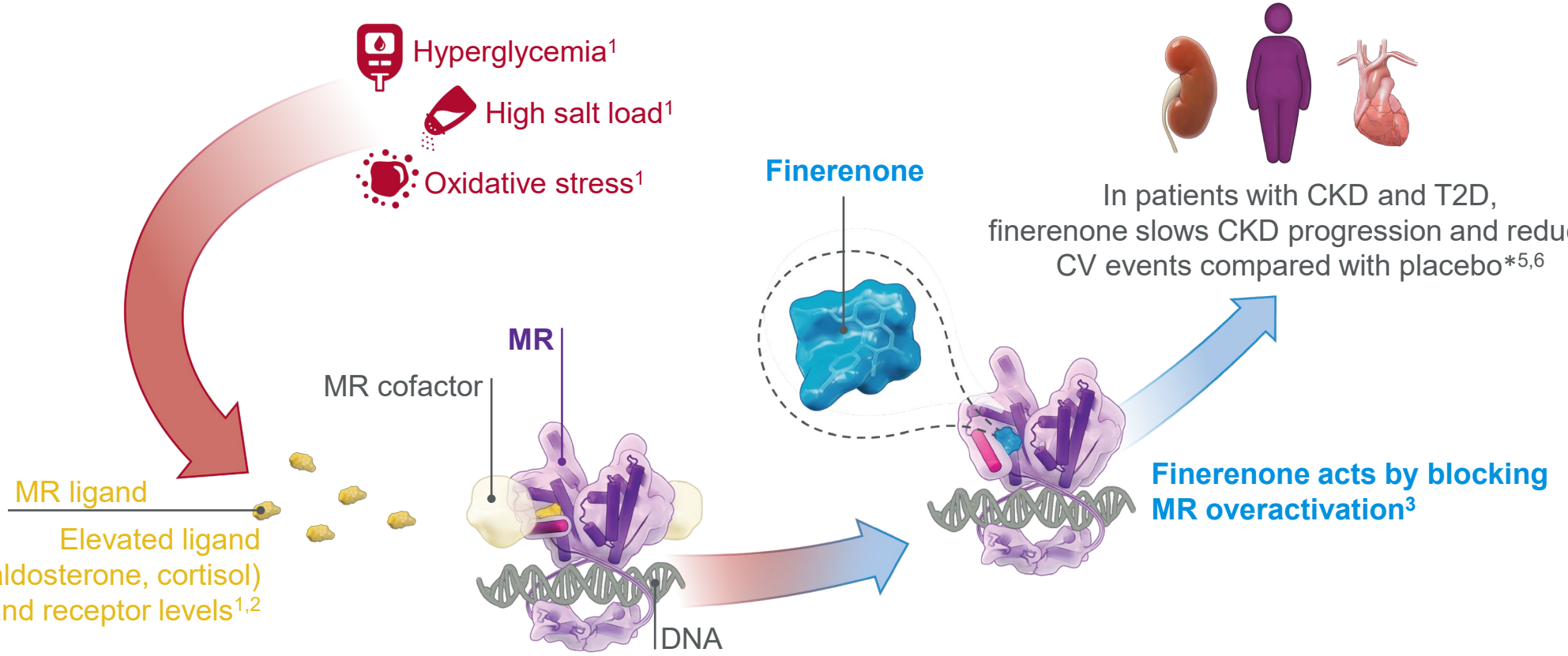


There is a need to find new therapies for patients with non-diabetic CKD

CKD, chronic kidney disease

1. GBD Chronic Kidney Disease Collaboration. *Lancet* 2020;395:709–733; 2. Webster AC, *et al*. *Lancet* 2017;389:1238–1252

Finerenone blocks MR overactivation which plays a role in CKD progression



*Efficacy was shown independent of the glycemic state and no effects on HbA1c were observed

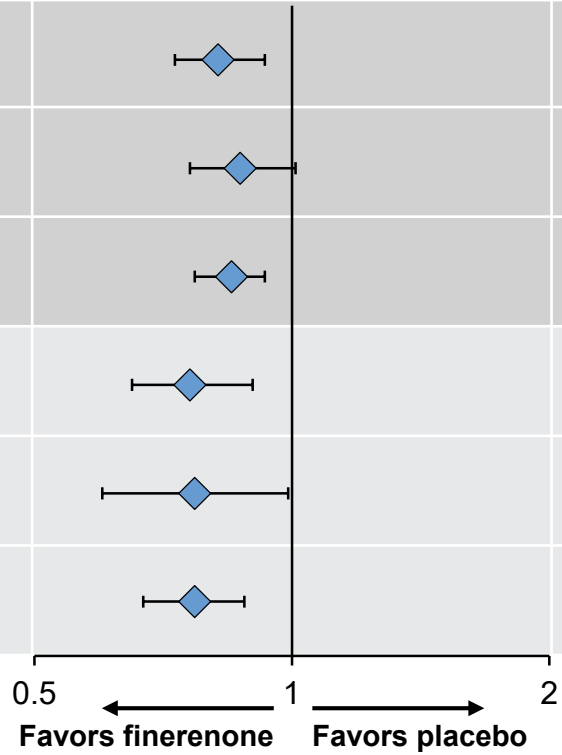
CV, cardiovascular; MR, mineralocorticoid receptor; T2D, type 2 diabetes

1. Buonafine M, *et al. Am J Hypertens* 2018;31:1165–1174; 2. Buglioni A, *et al. Hypertension* 2015;65:45–53; 3. Agarwal R, *et al. Nephrol Dial Transplant* 2020; doi: 10.1093/ndt/gfaa294; 4. Khan NUA & Movahed A. *Rev Cardiovasc Med* 2004;5:71–81; 5. Bakris GL, *et al. N Engl J Med* 2020;383:2219–2229; 6. Pitt B, *et al. N Engl J Med* 2021; doi: 10.1056/NEJMoa2110956

Finerenone reduced the risk of CKD progression in patients with CKD and T2D

Kidney outcomes in FIDELIO-DKD, FIGARO-DKD, and FIDELITY[1–3]

Kidney composite outcome	Trial and population (n finerenone/n placebo)	Finerenone n/100 PY	Placebo n/100 PY	HR (95% CI)		*p*-value
Kidney composite outcome with ≥40% eGFR decline*	**FIDELIO-DKD (n=2833 / n=2841)[1]**	7.59	9.08		0.82 (0.73–0.93)	0.001
	FIGARO-DKD (n=3686 / n=3666)[2]	3.15	3.58		0.87 (0.76–1.01)	0.069[3]
	FIDELITY (n=6519 / n=6507)[4]	4.81	5.64		0.85 (0.77–0.93)	0.0004
Kidney composite outcome with ≥57% eGFR decline#	**FIDELIO-DKD (n=2833 / n=2841)[1]**	3.64	4.74		0.76 (0.65–0.90)	–
	FIGARO-DKD (n=3686 / n=3666)[2]	0.95	1.23		0.77 (0.60–0.99)	0.041[3]
	FIDELITY (n=6519 / n=6507)[4]	1.96	2.55		0.77 (0.67–0.88)	0.0002

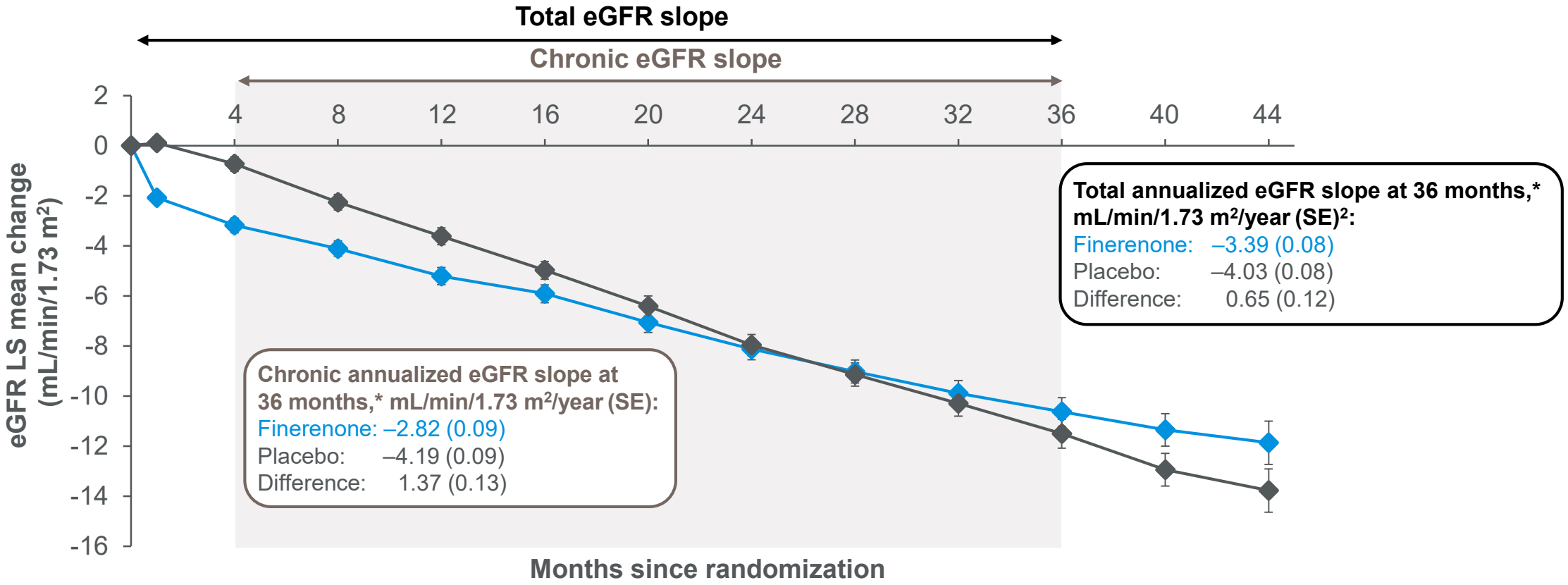


*Composite of time to kidney failure, sustained ≥40% decrease in eGFR from baseline, or renal death; kidney failure defined as either ESKD (initiation of chronic dialysis for ≥90 days or kidney transplant) or sustained decrease in eGFR <15 mL/min/1.73 m^2; #composite of time to kidney failure, sustained ≥57% decrease in eGFR from baseline, or renal death

CI, confidence interval; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HR, hazard ratio; PY, patient-years

1. Bakris GL, *et al. N Engl J Med* 2020;383:2219–2229; 2. Pitt B, *et al. N Engl J Med* 2021; doi:10.1056/NEJMoa2110956; 3. Pitt B, presented at ESC Congress 2021 Hot Line session 28 August 2021; available at https://esc365.escardio.org/presentation/239054 [accessed19 Oct 2021]; 4. Filippatos G and Agarwal A, presented at ESC Congress 2021 Hot Line session 28 August 2021; available at https://esc365.escardio.org/presentation/239704 [accessed 26 Oct 2021]

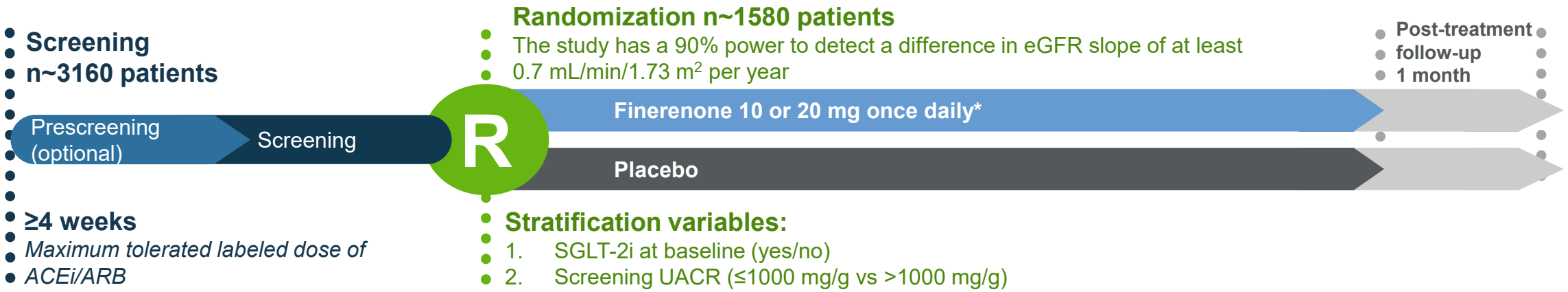
Finerenone attenuated decline in eGFR in FIDELIO-DKD[1] and informed the design of FIND-CKD



In FIDELIO-DKD, the effects of finerenone on total and chronic eGFR slope at 36 months translated into benefits on the primary[#2] and secondary[‡] kidney composite endpoints

*Two-slope mixed model for repeated measures. Reference: Vonesh E, *et al*. *Stat Med* 2019;38:4218–4239. doi: 10.1002/sim.8282; [#]time to kidney failure, sustained ≥40% decrease in eGFR from baseline, or renal death; [‡]time to CV death, non-fatal myocardial infarction, non-fatal stroke, or HHF
HHF, hospitalization for heart failure; LS, least-squares; SE, standard error
1. Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229; 2. Bayer AG. Data on file

FIND-CKD is a randomized, double-blind, placebo-controlled, parallel-group, multicenter phase III trial



Visits[#] Screening, baseline, month 1, month 3, then every 3 months up to month 12, and every 4 months thereafter. (A "hybrid" DCT model will be implemented where feasible and local laws/regulations allow)

Primary efficacy outcome	Secondary efficacy outcomes	Exploratory/supportive efficacy outcomes	Safety outcomes
• Annual mean rate of change in eGFR as measured by the total slope of eGFR (from baseline to month 32)	• Time to the composite of kidney failure, sustained ≥57% decrease in eGFR, HHF, or CV death • Time to the composite of kidney failure or sustained ≥57% decrease in eGFR • Time to the composite of HHF or CV death	• Chronic eGFR slope (from month 3 to end of planned treatment period) • eGFR change from baseline to 4 weeks off treatment	• Number of patients with treatment-emergent SAEs, treatment-emergent AEs, and AEs of special interest

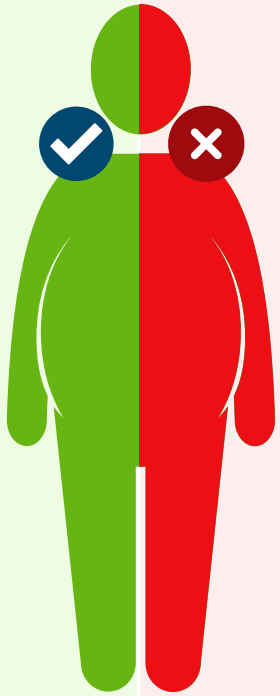
*Starting dose based on eGFR: 10 mg if eGFR <60 mL/min/1.73 m^2; 20 mg if eGFR ≥60 mL/min/1.73 m^2. The target dose of finerenone for all patients is 20 mg once daily, with titration based on serum potassium concentration and eGFR; [#]additional visits will take place 4 weeks after each up-titration, or treatment re-initiation after interruption for >7 days, and 1 month after the end of treatment

ACEi, angiotensin-converting enzyme inhibitor; AE, adverse event; ARB, angiotensin receptor blocker; DCT, decentralized clinical trial; R, randomization; SAE, serious adverse event; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; UACR, urine albumin-to-creatinine ratio

Eligible patients are those with non-diabetic CKD, treated with a maximum tolerated labeled dose of an ACEi or ARB

Inclusion criteria

- Aged ≥18 years with CKD
- On stable and maximum tolerated labeled dose of ACEi or ARB for ≥4 weeks
- UACR at screening ≥200–≤3500 mg/g and eGFR≥25–90 mL/min/1.73 m^2*
- Serum [K^+] ≤4.8 mmol/L



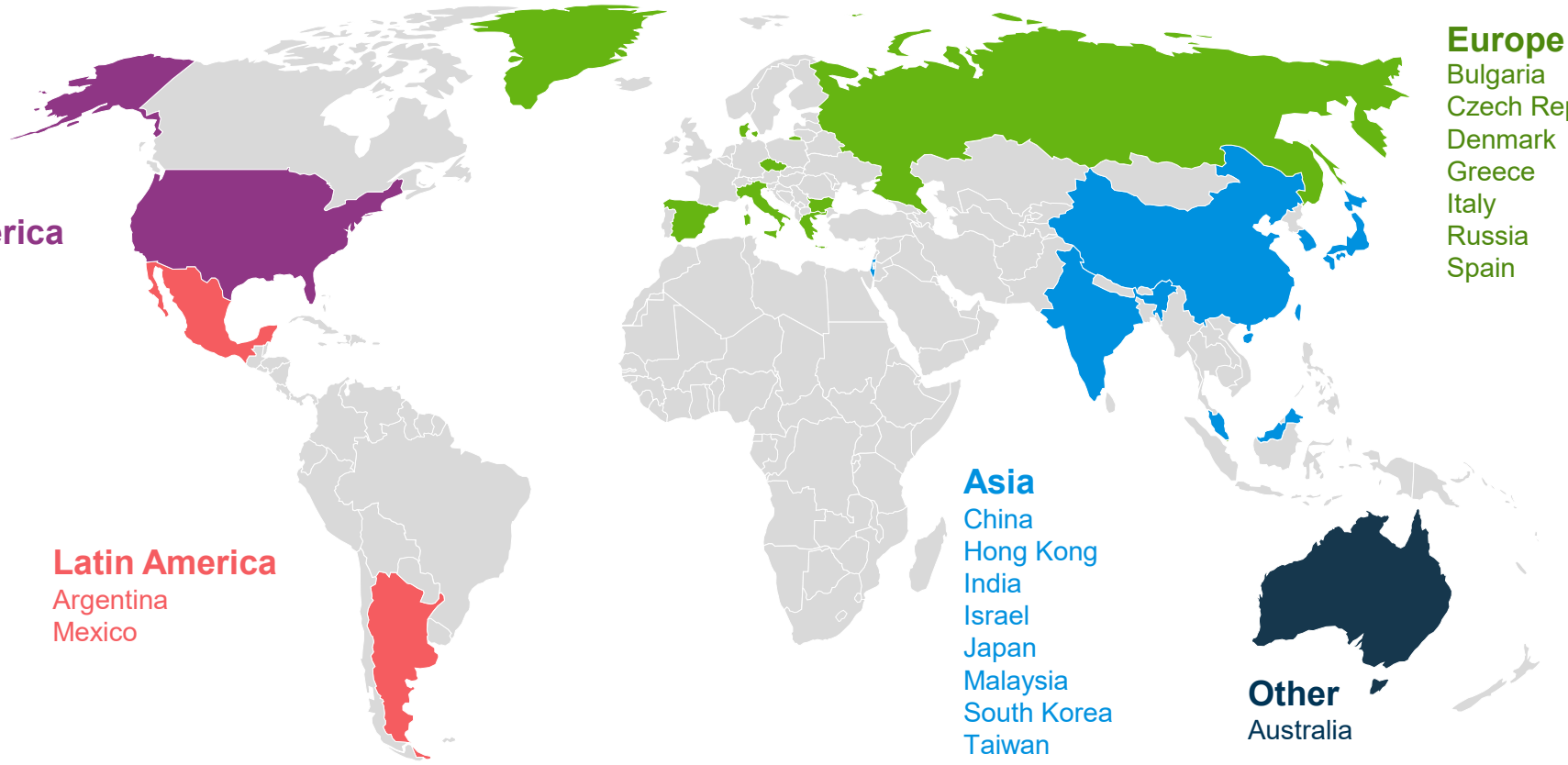
Key exclusion criteria

- T1D or T2D
- HbA1c ≥6.5% (48 mmol/mol)
- Uncontrolled hypertension#
- Symptomatic HFrEF with class 1A recommendation for treatment with a steroidal MRA
- Recent or ongoing immunosuppressive therapy
- Other kidney disease‡

*Either UACR ≥200–<500 mg/g with eGFR ≥25–<60 mL/min/1.73 m^2 or UACR ≥500–≤3500 mg/g with eGFR ≥25–<90 mL/min/1.73 m^2; to ensure a prespecified ratio for a population at risk of progressive renal function decline, the number of participants with eGFR 25–60 mL/min/1.73 m^2 and UACR ≥200 and <500 mg/g is planned to be capped at approximately 10% of the total population; #mean sitting SBP ≥160 mmHg or mean sitting DBP ≥100 mmHg at the screening visit; ‡known autosomal recessive/dominant polycystic kidney disease or lupus nephritis or anti-neutrophil cytoplasmic antibody-associated vasculitis within 6 months prior to screening

DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; HFrEF, heart failure with reduced ejection fraction; [K^+], potassium concentration; MRA, mineralocorticoid receptor antagonist; SBP, systolic blood pressure; T1D, type 1 diabetes

FIND-CKD is enrolling patients with non-diabetic CKD across ~270 centers from 19 countries worldwide



North America
United States

Latin America
Argentina
Mexico

Asia
China
Hong Kong
India
Israel
Japan
Malaysia
South Korea
Taiwan

Other
Australia

Europe
Bulgaria
Czech Republic
Denmark
Greece
Italy
Russia
Spain

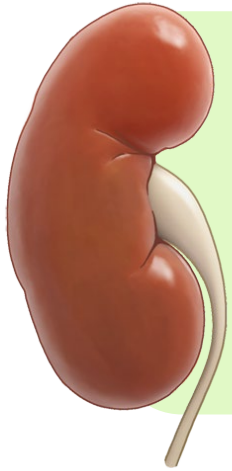
Study start date:
Sep 2021[1]

Estimated completion date:
Dec 2025[1]

1. Bayer. https://clinicaltrials.gov/ct2/show/NCT05047263 [accessed 7 Oct 2021]

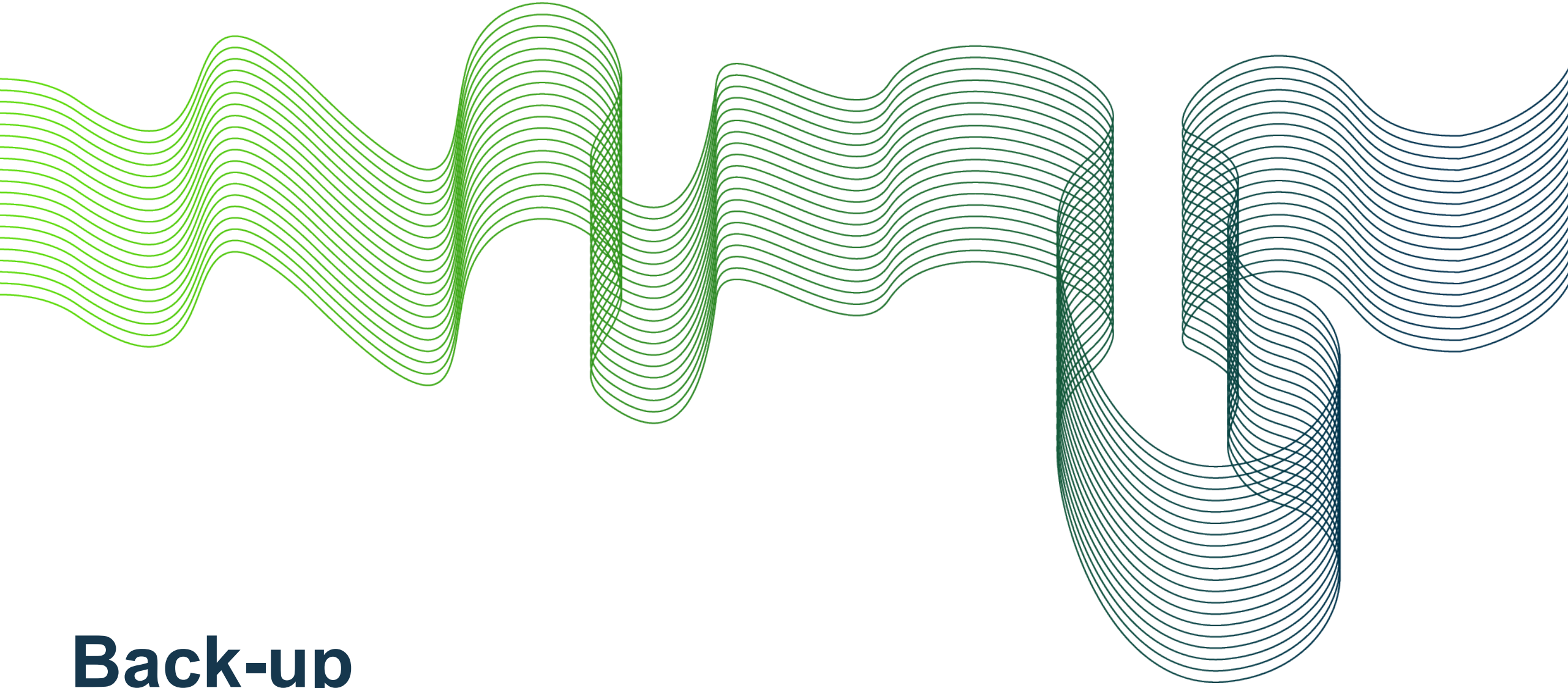
Conclusions

- FIDELIO-DKD and FIGARO-DKD demonstrated benefits of finerenone for kidney and cardiovascular protection in patients with CKD and T2D[1,2]



FI**ND-CKD** will determine whether finerenone can provide kidney protection to patients with CKD *without* diabetes who are on optimal medical therapies

1. Bakris GL, *et al. N Engl J Med* 2020;383:2219–2229; 2. Pitt B, *et al. N Engl J Med* 2021; doi: 10.1056/NEJMoa2110956



Back-up