DukeHeart *On The Go*

FIDELITY Analyses: Finerenone and Cardiorenal Outcomes by History of Cardiovascular Disease in Patients With Type 2 Diabetes

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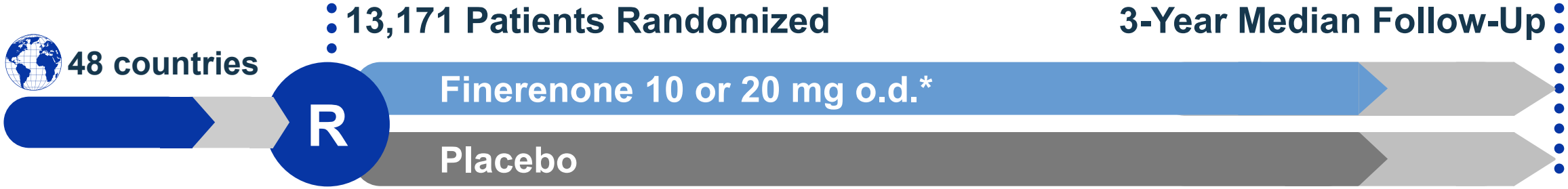
MedEd ON THE GO

FIDELITY Is a Large, Pooled Trial Dataset With Prespecified Analyses of the FIDELIO-DKD and FIGARO-DKD Trials[1–3]



*10 mg if screening eGFR 25–<60 mL/min/1.73 m^2, 20 mg if ≥60 mL/min/1.73 m^2; up-titration encouraged from month 1 if serum [K+] ≤4.8 mEq/L and eGFR stable; #kidney failure defined as either ESKD (initiation of chronic dialysis for ≥90 days or kidney transplant) or an eGFR <15 mL/min/1.73 m^2

CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalization for heart failure; [K+], potassium concentration; MI, myocardial infarction; o.d., once daily; RASi, renin–angiotensin–aldosterone system inhibitor; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio

1. Agarwal R, et al. *Eur Heart J.* 2022;43(6):474–484; 2. Bakris GB, et al. N *Engl J Med.* 2020;383(23):2219–2229; 3. Pitt B, et al. *N Engl J Med.* 2021;385(24):2252–2263.

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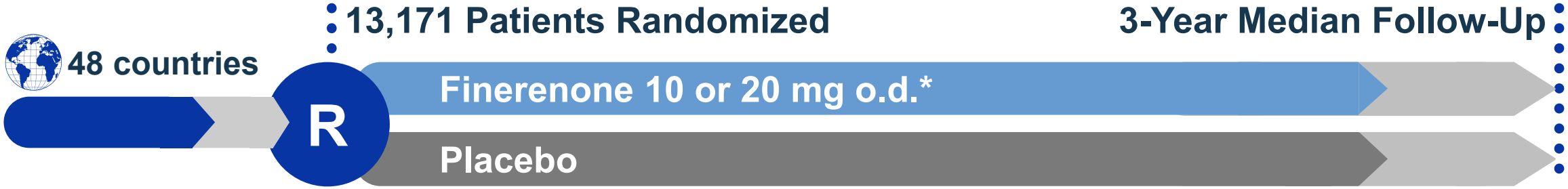
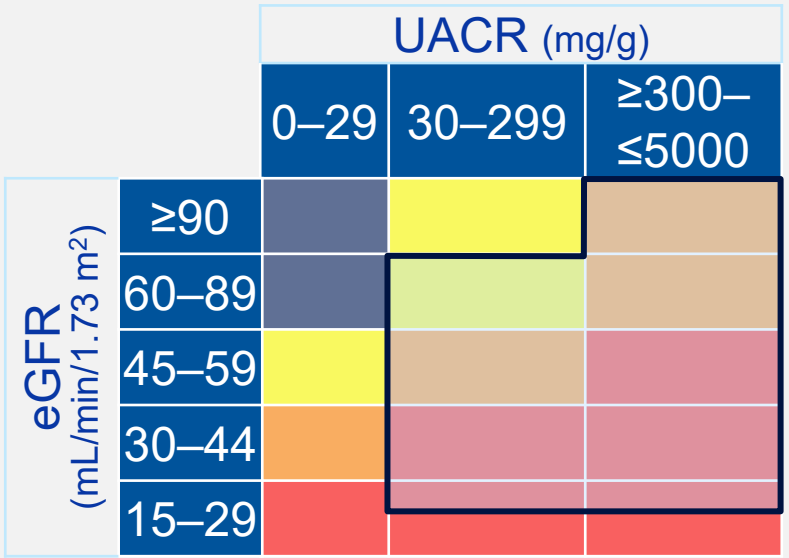


Key Eligibility Criteria

- ✓ T2D
- ✓ CKD
- ✓ On Single RASi
- ✓ Serum [K^+] ≤4.8 mmol/L
- ✗ Symptomatic HFrEF



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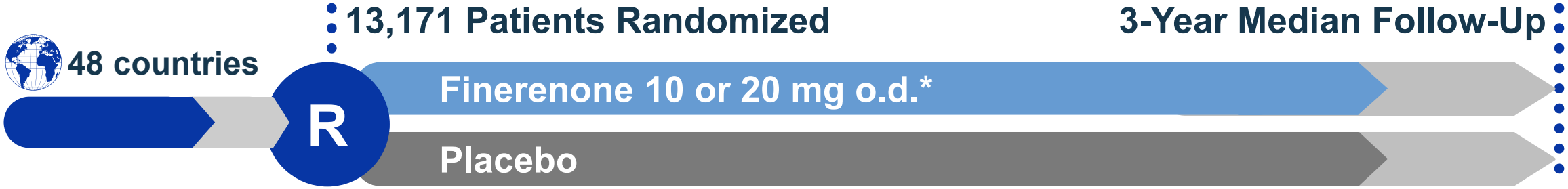

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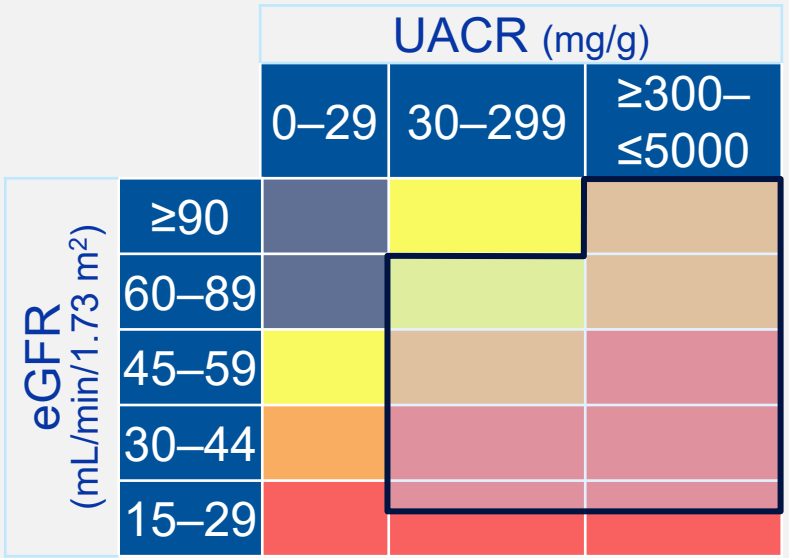
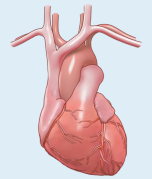


Key Outcomes

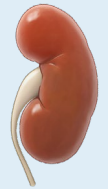
CV Composite

Time to CV death, nonfatal MI, nonfatal stroke, or HHF



≥57% eGFR Kidney Composite

Time to kidney failure,# sustained ≥57% decrease in eGFR from baseline, or kidney-related death



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This Prespecified Substudy of FIDELITY Evaluated the Efficacy and Safety of Finerenone on CV and Kidney Outcomes According to Medical History of ASCVD at Baseline

ASCVD was defined as investigator-reported medical history of at least one the following:

- CAD
- Previous MI
- Coronary revascularization (PCI or CABG)
- Previous ischemic stroke
- Angiographically proven stenosis ≥50% in ≥1 major coronary artery
- PAD
- Carotid endarterectomy

A history of HF was not included in the definition of ASCVD

*Time to first event of CV death, nonfatal MI, nonfatal stroke, or HHF; #time to kidney failure (ESKD or an eGFR <15 ml/min/1.73 m2), sustained ≥57% decrease in eGFR from baseline, or renal death
ASCVD, atherosclerotic cardiovascular disease; CABG, coronary artery bypass graft; CAD, coronary artery disease; CI, confidence interval; ESKD, end-stage kidney disease; HF, heart failure; HR, hazard ratio; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; PY, patient-years.

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Incidence of Composite CV Outcome, CV Death or HHF, and All-Cause Mortality Was Higher in Patients With Vs. Without Prevalent ASCVD

Outcome	History of ASCVD				HR (95% CI)
	With (n=5935)		Without (n=7091)		
	n (%)	n per 100 PY	n (%)	n per 100 PY	
Composite CV Outcome*	1106 (18.6)	**6.9**	658 (9.3)	**3.0**	2.09 (1.89–2.30)
CV Death or HHF	753 (12.7)	**4.5**	426 (6.0)	**1.9**	2.12 (1.88–2.40)
Composite Kidney Outcome#	328 (5.5)	**2.1**	497 (7.0)	**2.4**	0.96 (0.83–1.10)
All-Cause Mortality	695 (11.7)	**4.0**	471 (6.6)	**2.1**	1.72 (1.52–1.94)

*Time to first event of CV death, nonfatal MI, nonfatal stroke, or HHF; #time to kidney failure (ESKD or an eGFR <15 ml/min/1.73 m2), sustained ≥57% decrease in eGFR from baseline, or renal death
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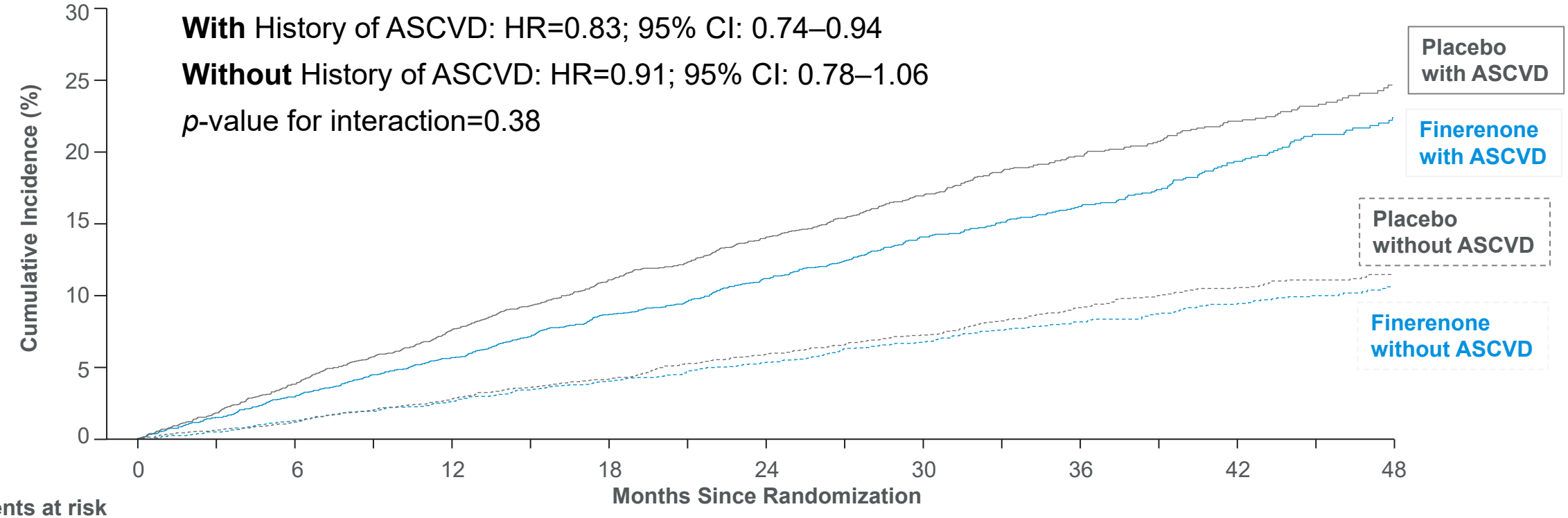
CV Benefit of Finerenone Not Modified by Prevalent ASCVD Status

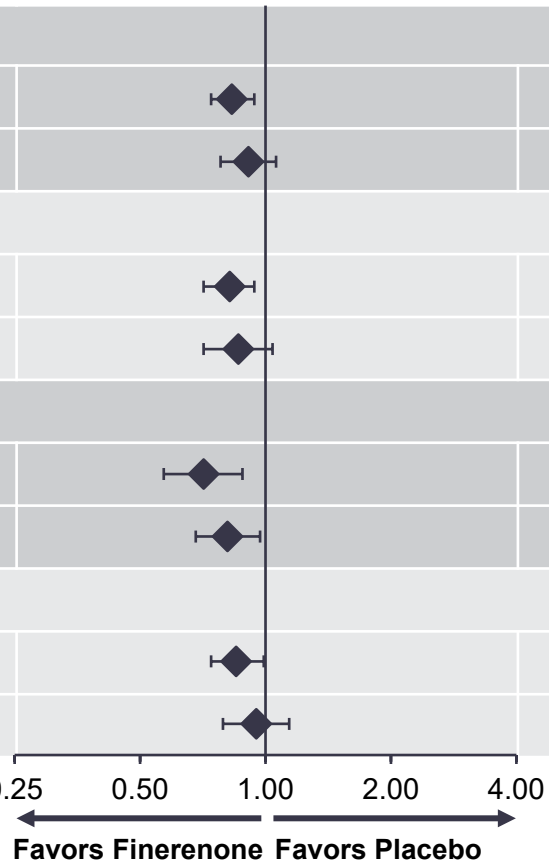
Time to CV Death, Nonfatal MI, Nonfatal Stroke, or HHF



No. of patients at risk								
Finerenone with ASCVD	2979	2883	2783	2662	2294	1766	1185	766	366
Placebo with ASCVD	2956	2835	2698	2578	2208	1678	1122	729	334
Finerenone without ASCVD	3540	3477	3419	3347	2979	2441	1880	1421	721
Placebo without ASCVD	3551	3495	3427	3360	2976	2469	1847	1406	748

Finerenone Reduced the Risk of Composite CV and Kidney Outcomes as well as CV Death and HHF Compared to Placebo, Irrespective of History of ASCVD

Outcome	Finerenone		Placebo		HR (95% CI)	*p*-value for interaction
	n (%)	N per 100 PY	n (%)	N per 100 PY		
Composite CV Outcome*						
With a history of ASCVD	511 (17.2)	6.3	595 (20.1)	7.6	0.83 (0.74–0.94)	0.38
Without a history of ASCVD	314 (8.9)	2.9	344 (9.7)	3.2	0.91 (0.78–1.06)	
CV Death or HHF						
With a history of ASCVD	342 (11.5)	4.1	411 (13.9)	5.0	0.82 (0.71–0.94)	0.68
Without a history of ASCVD	197 (5.6)	1.8	229 (6.4)	2.1	0.86 (0.71–1.04)	
Composite Kidney Outcome#						
With a history of ASCVD	139 (4.7)	1.7	189 (6.4)	2.4	0.71 (0.57–0.88)	0.33
Without a history of ASCVD	221 (6.2)	2.1	276 (7.8)	2.7	0.81 (0.68–0.97)	
All-Cause Mortality						
With a history of ASCVD	323 (10.8)	3.7	372 (12.6)	4.4	0.85 (0.74–0.99)	0.38
Without a history of ASCVD	229 (6.5)	2.0	242 (6.8)	2.2	0.95 (0.79–1.14)	



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The Risk of Hyperkalemia Was Higher With Finerenone, Irrespective of ASCVD History, but Discontinuation due to Hyperkalemia Was Low

TEAE, %	With History of ASCVD		Without History of ASCVD	
	Finerenone (n=2974)	Placebo (n=2950)	Finerenone (n=3536)	Finerenone (n=3539)
Any SAE	34.4	36.8	29.4	31.1
Treatment related	1.5	1.1	1.0	0.8
Leading to treatment discontinuation	2.4	2.3	2.1	2.5
Serious Hyperkalemia	1.4	0.3	0.8	0.2
Treatment related	1.0	0.1	0.4	0.1
Leading to hospitalization	**1.2**	**0.1**	**0.7**	**0.2**
Leading to treatment discontinuation	**0.2**	**<0.1**	**0.1**	**0**

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Leading to treatment discontinuation	2.4	2.3	2.1	2.5
Serious Hyperkalemia	1.4	0.3	0.8	0.2
Treatment related	1.0	0.1	0.4	0.1
Leading to hospitalization	**1.2**	**0.1**	**0.7**	**0.2**
Leading to treatment discontinuation	**0.2**	**<0.1**	**0.1**	**0**

Summary:

In a patient population with CKD (stages 1–4 with moderate to severely elevated albuminuria) and T2D, with well-controlled blood pressure and HbA1c and treated with a maximum tolerated dose of an RASi:

The risk of **adverse CV outcomes was higher in patients with ASCVD** compared to those without; however, **the risk of adverse kidney outcomes was similar** between groups

The CV and kidney benefits of finerenone compared to placebo were consistent, **irrespective of history of ASCVD**

The **safety profile of finerenone was similar** between patients **with and without a history** of ASCVD

Although **hyperkalemia** was increased with finerenone, the **clinical impact was minimal**

Finerenone has shown benefit in **primary and secondary prevention across the spectrum** of patients with CKD and T2D, with a **good safety profile**