Nonsteroidal MRAs: Latest Evidence of Cardiorenal Protection in CKD and T2D

medtelligence℠

FIDELIO-DKD Study Design

13,911 patients enrolled

Run-in (4–16 weeks) → Screening → **R**

5,734 patients randomized

- **Finerenone 10 or 20 mg od***
- **Placebo**

2.6 years of median follow-up

Key Inclusion Criteria

Adult patients with CKD associated with T2D

UACR of 30 to 300 mg/g, eGFR 25 to 60 mL/min/1.73 m^2 and diabetic retinopathy

UACR of ≥300 mg/g and an eGFR of 25 to 75 mL/min/1.73 m^2

On maximum tolerated dose of RAAS inhibitor for ≥4 weeks

Serum potassium ≤4.8 mmol/L

Key Exclusion Criteria

Patients with known, significant nondiabetic kidney disease

Clinical diagnosis of chronic heart failure with reduced ejection fraction and persistent symptoms (NYHA class II-IV)

Key Outcomes[1,2]

Kidney composite

- Time to kidney failure, sustained ≥40% decrease in eGFR from baseline, or renal death

CV composite

- Time to CV death, nonfatal MI, nonfatal stroke, or hospitalization for heart failure

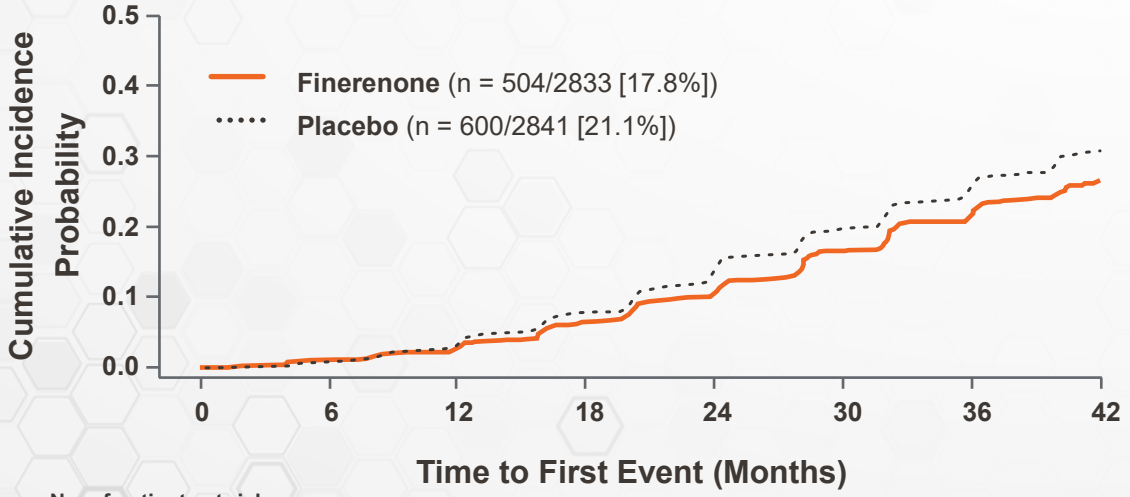
- ACEI/ARB optimized over 4- to 16-week run-in period
- Patients with heart failure with reduced ejection fraction were excluded

*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 potassium ≤4.8 mmol/L and eGFR stable.
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; NYHA, New York Heart Association; T2D, type 2 diabetes; UACR, urinary albumin-to-creatinine ratio.

1. Bakris GL, et al. *Am J Nephrol*. 2019;50(5):333-344. 2. Bakris GL, et al. *N Engl J Med*. 2020;383(23):2219-2229.

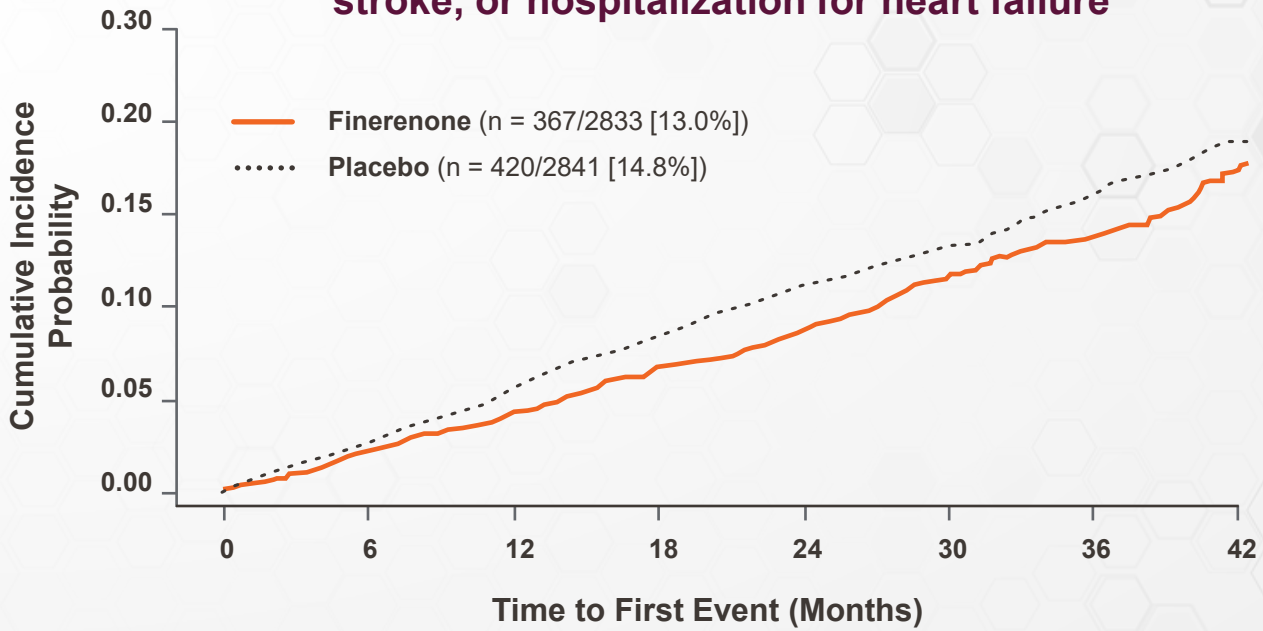
Finerenone significantly slowed CKD progression and significantly reduced the risk of the CV composite endpoint[1,2]

Primary composite endpoint consisted of a sustained decline in eGFR of ≥40%, kidney failure,* or renal death



No. of patients at risk								
Finerenone	2833	2705	2607	2397	1808	1274	787	441
Placebo	2841	2724	2586	2379	1758	1248	792	453

Secondary composite endpoint consisted of CV death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure



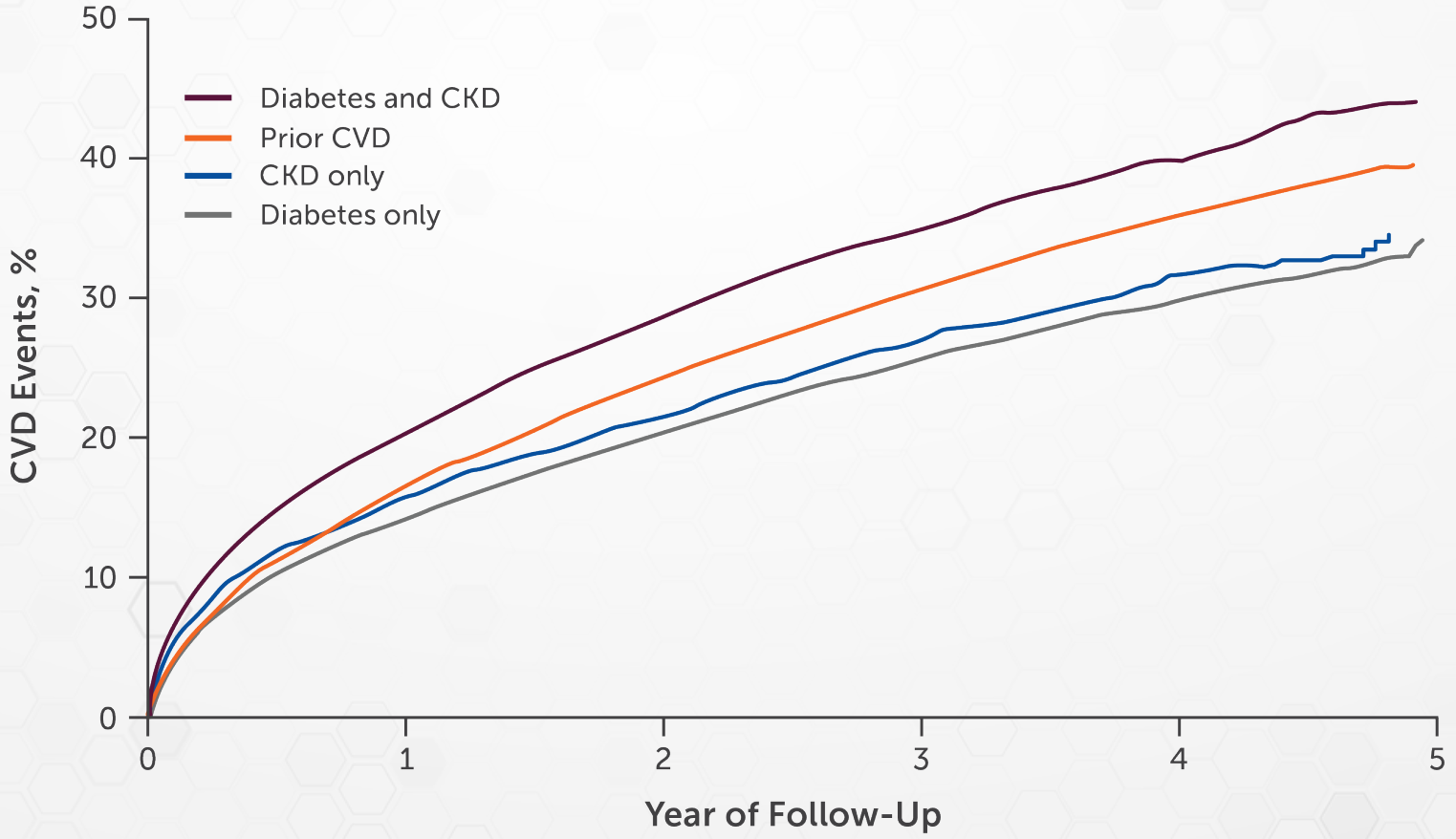
No. of patients at risk								
Finerenone	2833	2760	2688	2582	2017	1488	984	537
Placebo	2841	2753	2653	2549	1969	1475	951	536

*Kidney failure was defined as chronic kidney dialysis or kidney transplantation, or a sustained decrease in eGFR to <15 mL/min/1.73 m^2.

CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate.

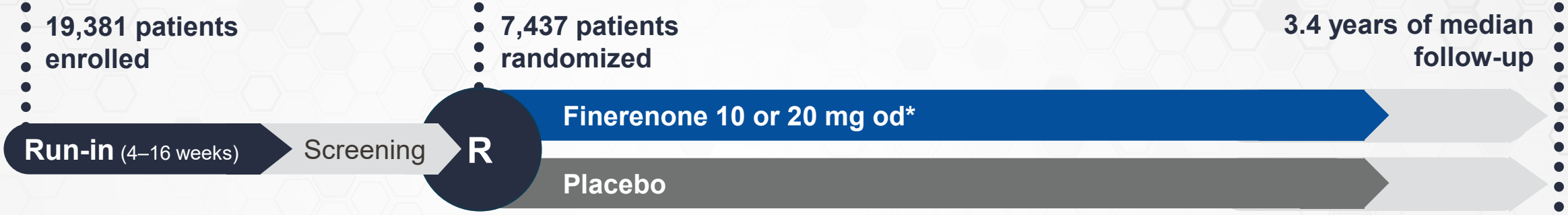
1. Kerendia (finerenone). Package insert. Bayer Healthcare Pharmaceuticals, Inc.; 2021. 2. Bakris GL, et al. *N Engl J Med.* 2020;383(23):2219-2229.

Diabetes with CKD Is a CVD Risk Accelerator



Hubbard D, et al. *Cardiovasc Diabetol*. 2021;20(1):58.

FIGARO-DKD: Study Design



Key Inclusion Criteria

Aged ≥18 years with T2D

eGFR ≥25 mL/min/1.73 m^2

UACR ≥30 – ≤5000 mg/g

On maximum tolerated dose of RAAS inhibitor for ≥4 weeks

Serum potassium ≤4.8 mmol/L

Key Exclusion Criteria

HFrEF with NYHA Class II-IV

Uncontrolled arterial hypertension

HbA1c >12%

Other kidney disease

Key Outcomes

CV composite

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

≥40% and ≥57% eGFR kidney composites

Time to kidney failure, sustained ≥40% or ≥57% decrease in eGFR from baseline, or renal death

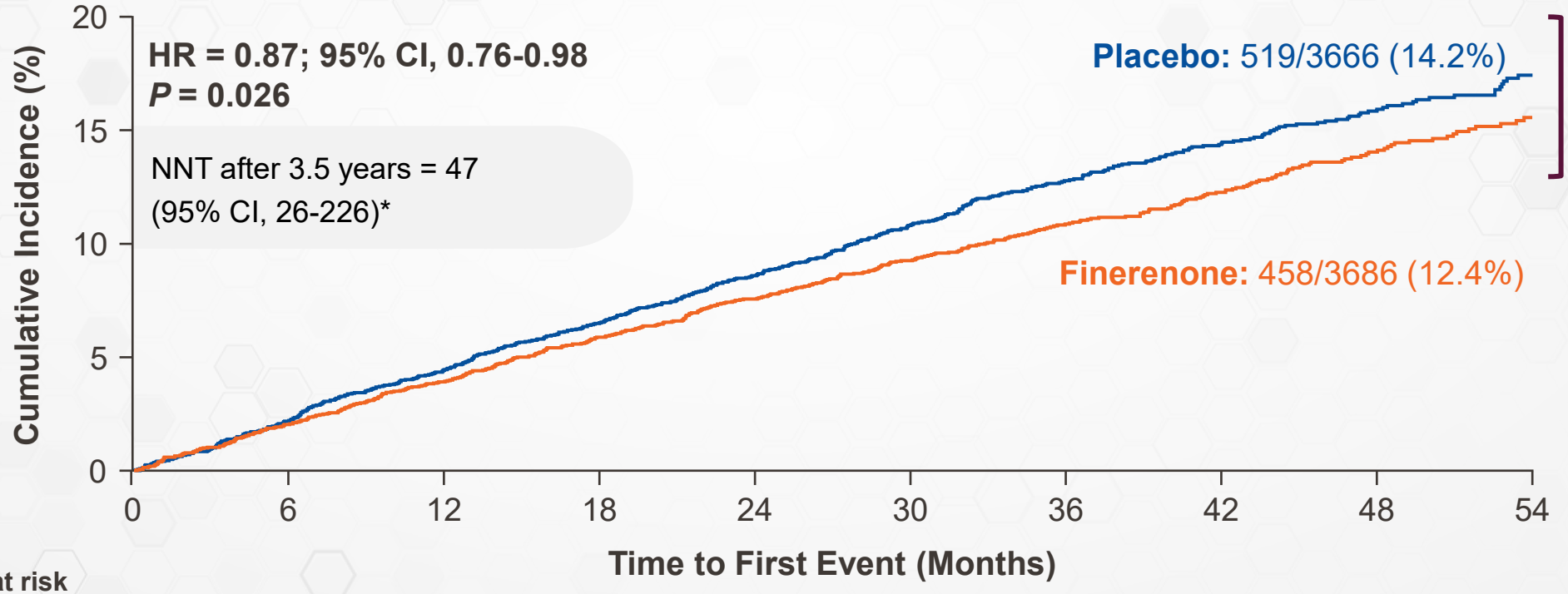
*10 mg if screening eGFR 25–<60 mL/min/1.73 m^2; 20 mg if ≥60 mL/min/1.73 m^2, up-titration encouraged from month 1 if serum potassium ≤4.8 mmol/L and eGFR stable. For further information, please consult the trial slides presented at ESC available as a resource to this activity.

CV, cardiovascular; eGFR, estimated glomerular filtration rate; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalization for heart failure; MI, myocardial infarction; NYHA, New York Heart Association; RAAS, renin-angiotensin-aldosterone system; T2D, type 2 diabetes; UACR, urinary albumin-to-creatinine ratio.

Pitt B, et al. FIGARO-DKD Trial. Presented at ESC 2021.

Reduction in Risk of Primary CV Outcome

Primary CV Outcome: Time to CV death, nonfatal MI, nonfatal stroke, or HHF



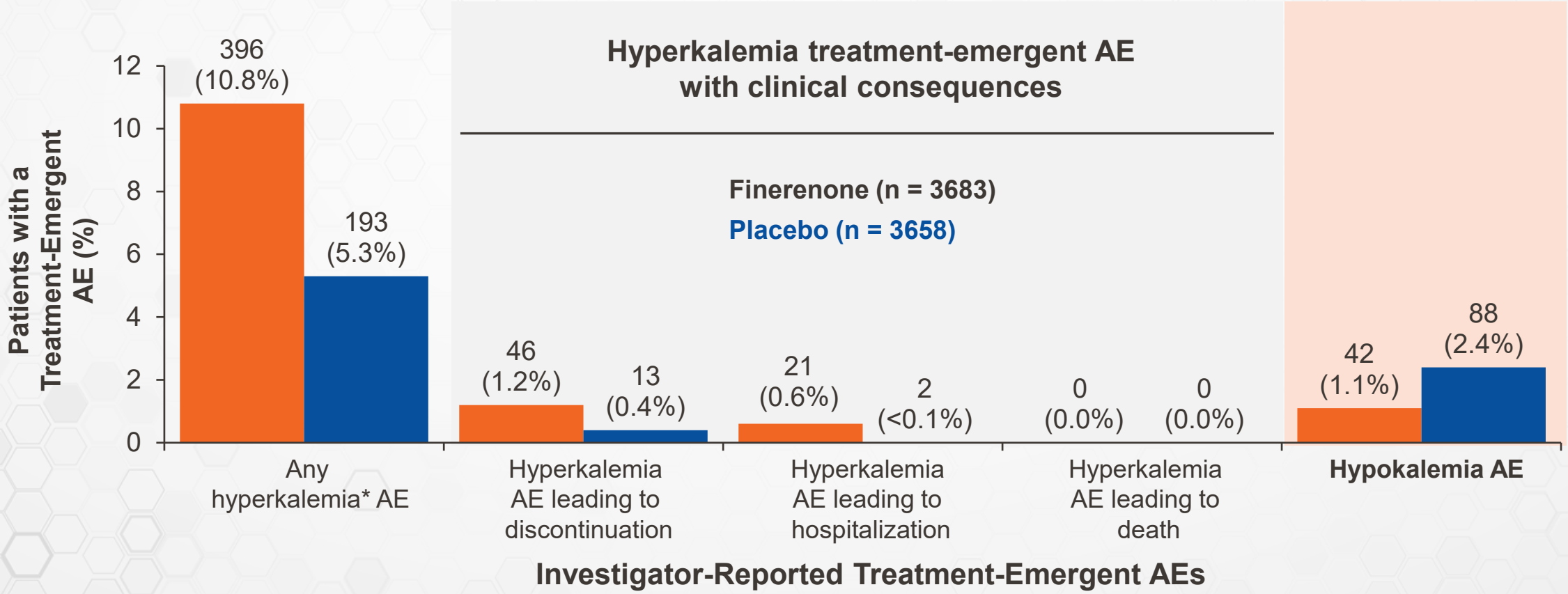
No. at risk										
Finerenone	3686	3600	3517	3427	3320	2781	2184	1712	1093	598
Placebo	3666	3577	3479	3389	3267	2730	2125	1657	1076	585

*NNT calculations based on an absolute risk reduction after 3.5 years of 2.1% (95% CI, 0.4-3.8). For further information, please consult the trial slides presented at ESC available as a resource to this activity.

CV, cardiovascular; HHF, hospitalization for heart failure; HR, hazard ratio; MI, myocardial infarction; NNT, number needed to treat.

Pitt B, et al. FIGARO-DKD Trial. Presented at ESC 2021.

Hyper- and Hypokalemia with Finerenone



*Investigator-reported AEs using the MedDRA preferred terms "hyperkalemia" and "blood potassium increased." For further information, please consult the trial slides presented at ESC available as a resource to this activity.

AE, adverse event; MedDRA, Medical Dictionary of Regulatory Activities.

Pitt B, et al. FIGARO-DKD Trial. Presented at ESC 2021.

Changes in Albuminuria and Subsequent Risk of Incident Chronic Kidney Disease

Prognosis of CKD by GFR and Albuminuria Categories

GFR categories (mL/min/1.73 m²) Description and range			Albuminuria categories Description and range		
			A1	A2	A3
			Normal to mildly increased	Moderately increased	Severely increased
			<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
G1	Normal or high	≥90			
G2	Mildly decreased	60-90			
G3a	Mildly to moderately decreased	45-59			
G3b	Moderately to severely decreased	30-44			
G4	Severely decreased	15-29			
G5	Kidney failure	<15			

Green, low risk (if no other markers of kidney disease, no CKD); Yellow, moderately increased risk; Orange, high risk; Red, very high risk. (KDIGO 2020)

3.5 million US veterans

- eGFR ≥ 60 mL/min/1.73 m²
- Mean age 64 years
- 97% male
- 91% diabetic

56,946 Final cohort

	1-year change in albuminuria	Incident CKD	Rapid eGFR decline
Decrease	> 2 fold	0.82 *(0.77-0.89)*	0.86 *(0.78-0.94)*
Decrease	1.25-2 fold	0.93 *(0.86-1.00)*	0.98 *(0.89-1.07)*
Increase	1.25-2 fold	1.12 *(1.05-1.20)*	1.18 *(1.08-1.29)*
Increase	> 2 fold	1.29 *(1.21-1.38)*	1.67 *(1.54-1.81)*

Conclusion: Relative changes in albuminuria over a 1-year interval were associated with subsequent risk of incident CKD.

1. National Kidney Foundation. https://www.kidney.org/kidneydisease/siemens_hcp_quickreference
2. Sumida K, et al. *Clin J Am Soc Nephrol.* 2017;12(12):1941-1949.