



# Finerenone Across CKM Stages: A Secondary Analysis of FIDELITY

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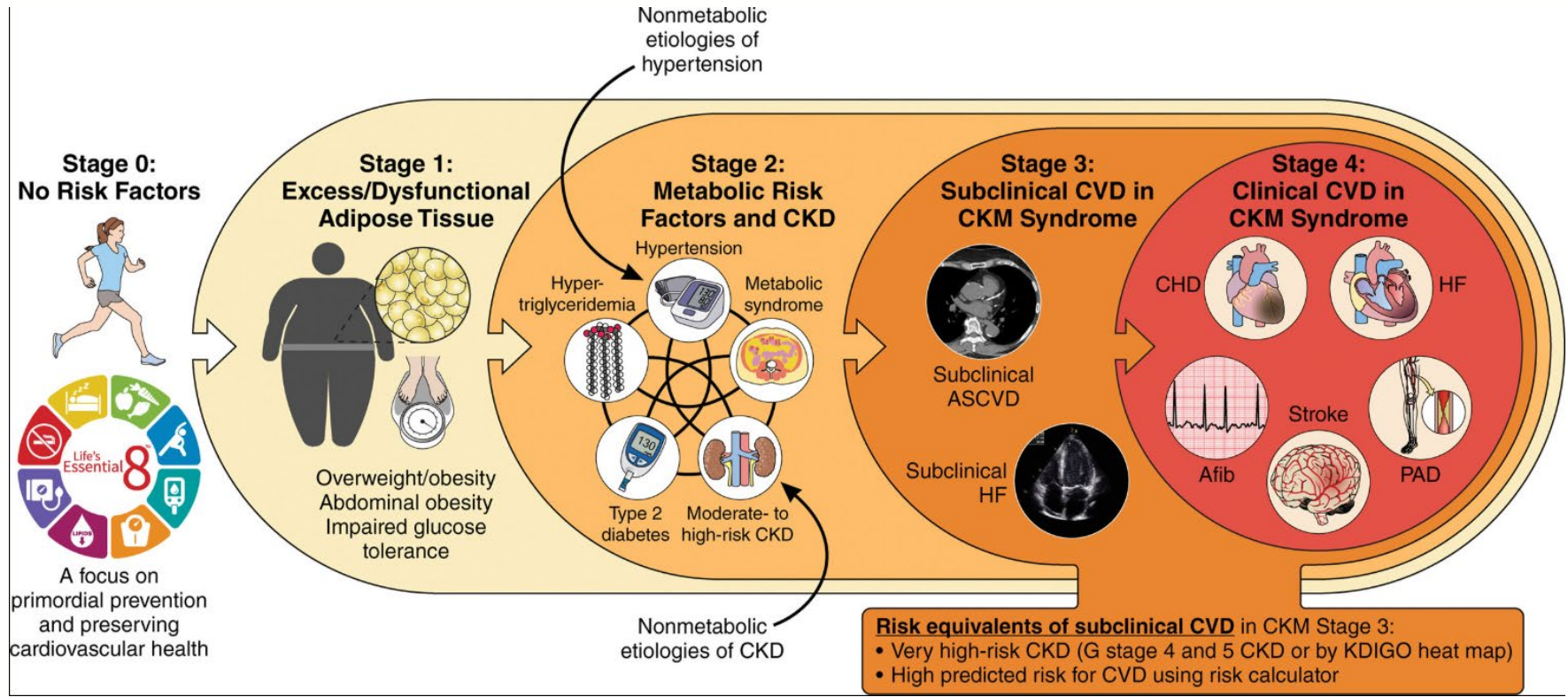
Harvard Medical School







# Disclosures

- FIDELITY (FIDELIO-DKD and FIGARO-DKD) was sponsored by Bayer AG

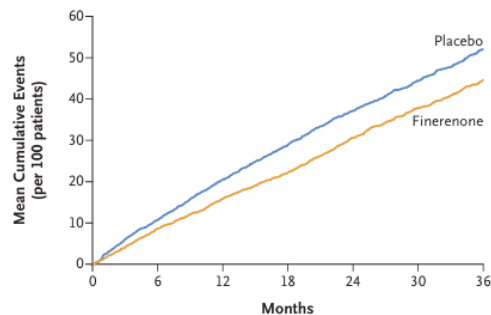
# Cardiovascular Kidney Metabolic (CKM) syndrome



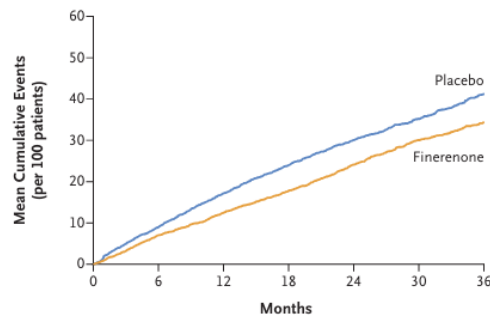
# Finerenone

Results					
	Endpoint CV composite	HR (95% CI)	p-value	Risk ↓	
		0.86 (0.78 – 0.95)	0.0018	14%	
	HHF	0.78 (0.66 – 0.92)	0.0030	22%	
	Kidney composite	HR (95% CI)	p-value	Risk ↓	
		0.77 (0.67 – 0.88)	0.0002	23%	
	Dialysis	0.80 (0.64 – 0.99)	0.040	20%	

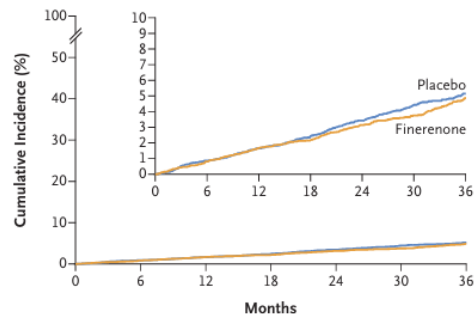
**A** Total Worsening Heart Failure Events and Death from Cardiovascular Causes



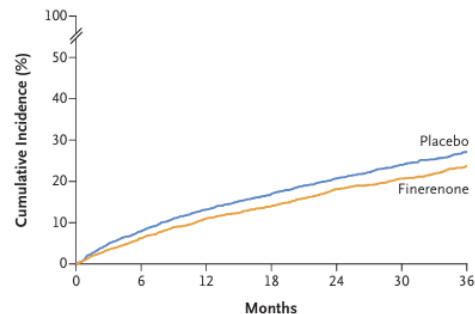
**B** Total Worsening Heart Failure Events



**C** Death from Cardiovascular Causes



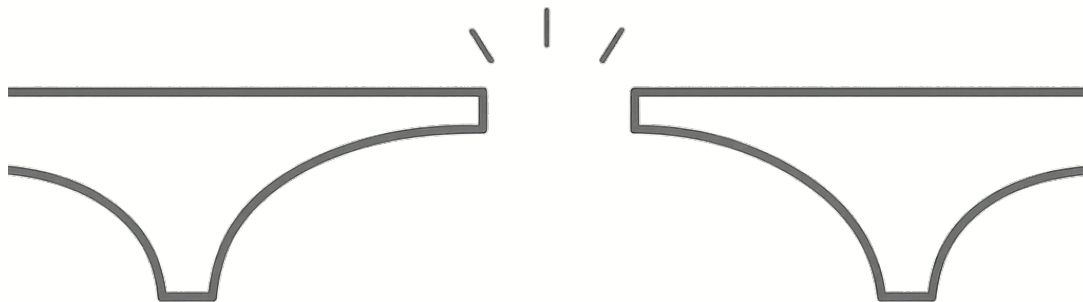
**D** First Worsening Heart Failure Event or Death from Cardiovascular Causes



Agarwal et al., Eur Heart J. 2021  
Solomon et al., NEJM. 2024

**CVCT**

# Gaps



- Limited data on **prognostic** value of CKM staging
- Unclear **feasibility** and **progression** of CKM stages in trials
- Limited evidence on finerenone's effects **across CKM stages**

# Methods

## Study population:

FIDELITY full analysis pooled cohort n=12,990



- T2D+CKD
- $\text{eGFR} \geq 25 \text{ ml/min/1.73m}^2$
- Serum  $\text{K} \leq 4.8 \text{ mmol/L}$
- Maximally tolerated RASi
- Excluding: symptomatic HFrEF

## Primary Outcomes:

### cardiovascular composite:



- CV death,
- non-fatal MI,
- non-fatal stroke
- HFH

### kidney composite:



- kidney failure
- $\geq 5\%$  decrease in eGFR over  $\geq 4$  weeks
- renal death

# CKMstages

Stage 2: metabolic risk factors (e.g., type 2 diabetes) or moderate- to high-risk CKD by KDIGO

Stage 3: very high-risk CKD

Stage 4: clinical CVD

				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
GFR categories (ml/min/1.73 m <sup>2</sup> ) Description and range	G1	Normal or high	≥90	Screen 1	Treat 1	Treat 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat 3	Treat 3
	G4	Severely decreased	15–29	Treat* 3	Treat* 3	Treat 4+
	G5	Kidney failure	<15	Treat 4+	Treat 4+	Treat 4+

CKD is classified based on:

- Cause (C)
- GFR (G)
- Albuminuria (A)

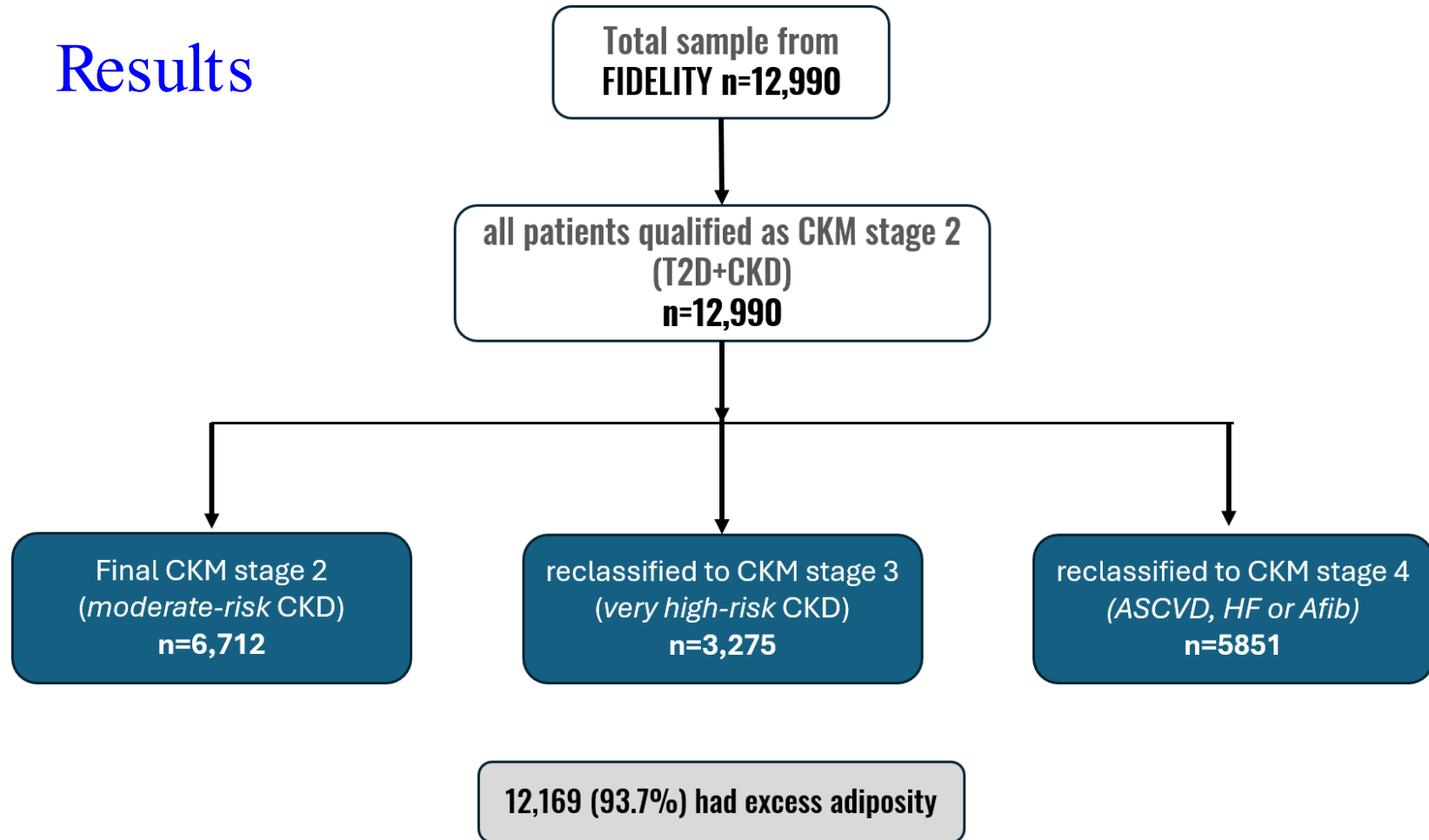
Low risk (if no other markers of kidney disease, no CKD)

Moderately increased risk

High risk

Very high risk

# Results





# Results

Clinical Outcomes  
by CKMstage

**Adjusted:** age, sex, smoking,  
treatment group

**Stratified:** study, region, eGFR,  
UACR, CVD history

Outcomes by CKMstage	aHR <sup>a</sup> (95% CI)	P value
Cardiac composite outcome/MACE <sup>a</sup>		
CKMstage2	Referent	
CKMstage3	1.05 (0.84, 1.29)	0.68
CKMstage4	1.87 (1.56, 2.24)	<0.001
Kidney composite outcome <sup>b</sup>		
CKMstage2	Referent	
CKMstage3	1.68 (1.22, 2.30)	0.001
CKMstage4	1.96 (1.43, 2.69)	<0.001
Cardiovascular death + heart failure hospitalizations		
CKMstage2	Referent	
CKMstage3	1.03 (0.79, 1.34)	0.84
CKMstage4	2.19 (1.75, 2.75)	<0.001
Cardiovascular death		
CKMstage2	Referent	
CKMstage3	1.16 (0.82, 1.63)	0.41
CKMstage4	2.05 (1.54, 2.72)	<0.001
Heart failure hospitalizations		
CKMstage2	Referent	
CKMstage3	1.08 (0.72, 1.61)	0.71
CKMstage4	2.99 (2.12, 4.24)	<0.001
All-cause mortality		
CKMstage2	Referent	
CKMstage3	1.07 (0.82, 1.38)	0.63
CKMstage4	1.79 (1.44, 2.22)	<0.001

# Results

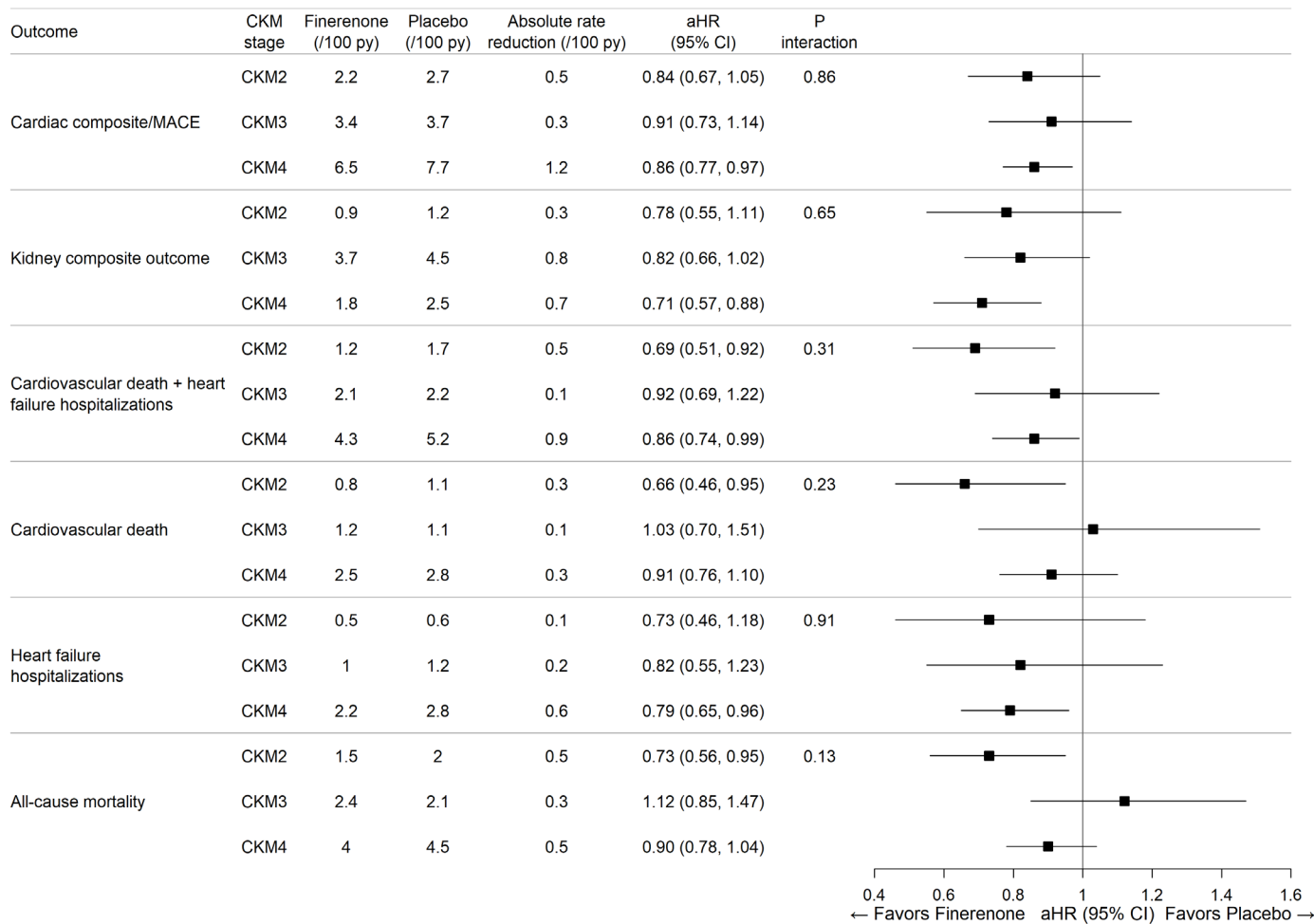
Sensitivity analysis in subset with NT-proBNP (n=1559)

reclassified 137 individuals from Stage 2 to 3

Outcomes by CKMstage	CKMstage baseline (per 100 py)	CKMstage with NTpro BNP (per 100 py)	Absolute diff	aHR <sup>a</sup> (95% CI) baseline CKMstage	aHR (95% CI) CKM stage with NT-proBNP
Cardiovascular composite/MACE					
CKMstage2	2.4 (1.7, 3.4)	1.1 (0.6, 2.0)	1.3	Referent	Referent
CKMstage3	3.9 (2.9, 5.2)	4.1 (3.3, 5.3)	0.2	0.80 (0.42, 1.52)	2.61 (1.19, 5.72)
CKMstage4	8.5 (7.3, 9.7)	8.5 (7.3, 9.7)	0	2.00 (1.13, 3.55)	5.10 (2.30, 11.30)
Kidney composite outcome <sup>b</sup>					
CKMstage2	1.3 (0.8, 2.1)	1.1 (0.6, 2.1)	0.2	Referent	Referent
CKMstage3	2.2 (1.5, 3.3)	2.0 (1.4, 2.9)	0.2	0.82 (0.28, 2.38)	1.75 (0.67, 4.58)
CKMstage4	2.3 (1.8, 3.0)	2.3 (1.8, 3.0)	0	1.17 (0.42, 3.25)	2.09 (0.72, 6.08)

# Results

## Treatment Effects of Finerenone by Baseline CKM Stage



# Results

## Safety events

Category	Safety events/treatment group:		
	Finerenone	Placebo	OR (95% CI) P <sub>interaction</sub>
Any serious adverse event			0.50
CKMstage 2	556 (29.1%)	580 (29.8%)	0.96 (0.84, 1.11)
CKMstage 3	494 (30.1%)	543 (33.5%)	0.85 (0.74, 0.99)
CKMstage 4	1024 (34.9%)	1081 (37.2%)	0.91 (0.82, 1.01)
Any adverse event leading to drug discontinuation			0.41
CKMstage 2	83 (4.3%)	79 (4.1%)	1.07 (0.78, 1.47)
CKMstage 3	121 (7.4%)	110 (6.8%)	1.09 (0.84, 1.43)
CKMstage 4	211 (7.2%)	161 (5.5%)	1.32 (1.07, 1.64)
Acute kidney injury			0.20
CKMstage 2	29 (1.5%)	46 (2.4%)	0.64 (0.40, 1.02)
CKMstage 3	65 (4.0%)	61 (3.8%)	1.05 (0.74, 1.50)
CKMstage 4	126 (4.3%)	127 (4.4%)	0.98 (0.76, 1.27)
Acute kidney injury leading to treatment discontinuation			0.50
CKMstage 2	2 (0.1%)	2 (0.1%)	1.02 (0.14, 7.22)
CKMstage 3	3 (0.2%)	4 (0.3%)	0.74 (0.16, 3.30)
CKMstage 4	9 (0.4%)	4 (0.2%)	2.23 (0.69, 7.25)

# Results

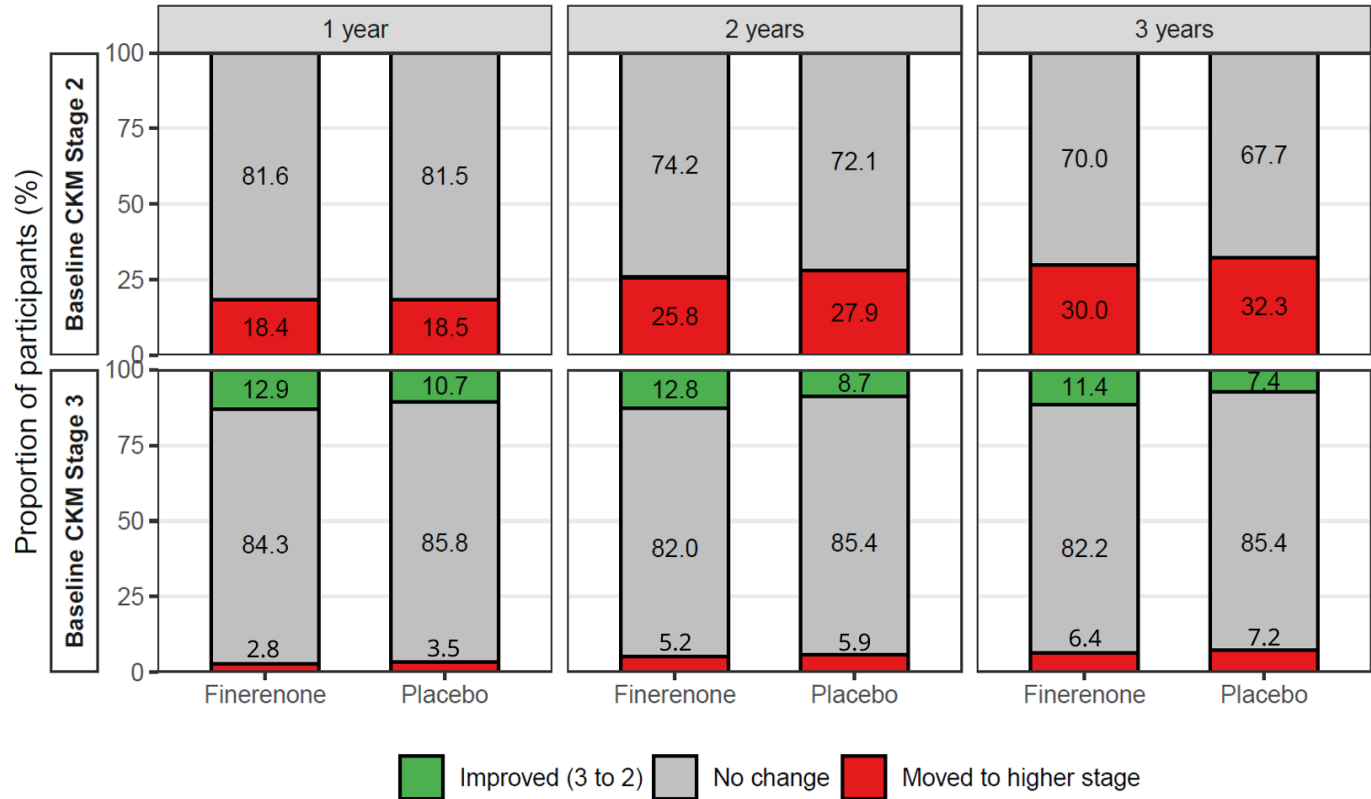
## Safety events

Category	Safety events/treatment group:		
	Finerenone	Placebo	OR (95% CI) P <sub>interaction</sub>
Hyperkalemia leading to treatment discontinuation			0.66
CKMstage 2	18 (0.9%)	4 (0.2%)	4.61 (1.56, 13.64)
CKMstage 3	37 (2.3%)	13 (0.8%)	2.85 (1.51, 5.38)
CKMstage 4	55 (1.9%)	21 (0.7%)	2.63 (1.59, 4.36)
Hyperkalemia leading to hospitalization			0.28
CKMstage 2	5 (0.3%)	1 (0.1%)	5.09 (0.59, 43.62)
CKMstage 3	21 (1.3%)	6 (0.4%)	3.49 (1.40, 8.66)
CKMstage 4	35 (1.2%)	3 (0.1%)	11.71 (3.60, 38.11)
Any serum potassium >5.5 mmol/L <sup>a</sup>			0.29
CKMstage 2	216 (11.4%)	106 (5.5%)	2.22 (1.74, 2.83)
CKMstage 3	364 (22.4%)	151 (9.4%)	2.78 (2.27, 3.41)
CKMstage 4	542 (18.7%)	258 (9.0%)	2.33 (1.99, 2.73)
Any serum potassium >6.0 mmol/L <sup>a</sup>			0.25
CKMstage 2	46 (2.4%)	18 (0.9%)	2.65 (1.53, 4.58)
CKMstage 3	80 (4.9%)	25 (1.6%)	3.27 (2.08, 5.16)
CKMstage 4	99 (3.4%)	49 (1.7%)	2.04 (1.44, 2.88)

# Results

## CKMStage Progression

regression from 3 to 2 OR	1.25; 95% CI (1.00, 1.56)	1.58; 95% CI (1.25, 1.99)	1.66; 95% CI (1.30, 2.13)
progression OR*	0.95; 95% CI (0.82, 1.10)	0.89; 95% CI (0.79, 1.01)	0.89; 95% CI (0.79, 1.00)



\*overall OR refers to participants with either stage 2 or 3 at baseline,

\*\*logistic regression adjusted for diabetes duration, smoking status, trial and region

# Limitations

relatively smaller number of patients in CKMstage 2 and 3

no CVrisk calculation performed to support CKMstaging (e.g., PREVENT)

potential under-classification of CKMstage 3

does not include CKMstage 1 by indication

# Insights

- CKM staging criteria broadly captured the patient population in this analysis
- Trials may have challenges in optimally classifying subclinical CVD (stage 3 CKM) given variable biomarker availability
- Improving kidney function may be a major avenue for CKM stage regression
- CV events remain the dominant driver of morbidity and mortality in CKM



End

Thank you!