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Impact of finerenone on chronic kidney disease progression in Chinese patients with type 2 diabetes

FIGARO-DKD subgroup analysis

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FIGARO-DKD
FInerenone in reducinG cArdiovascular moRtality and mOrbidity in DKD

Disclosures

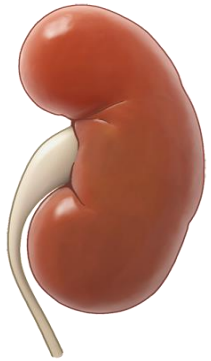
- **Katja Rohwedder** (presenter, on behalf of Ping Li) is a full-time employee of Bayer AG
- **Ping Li** has nothing to disclose

Finerenone provides a much-needed therapeutic option to the many Chinese patients with CKD

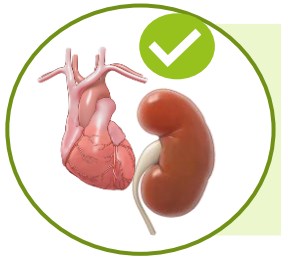
~82 million adults with **CKD in China**[1]

8.2%

estimated prevalence[1]



Chinese patients tend to **experience more rapid deterioration** in **kidney function** vs Caucasian patients[2]



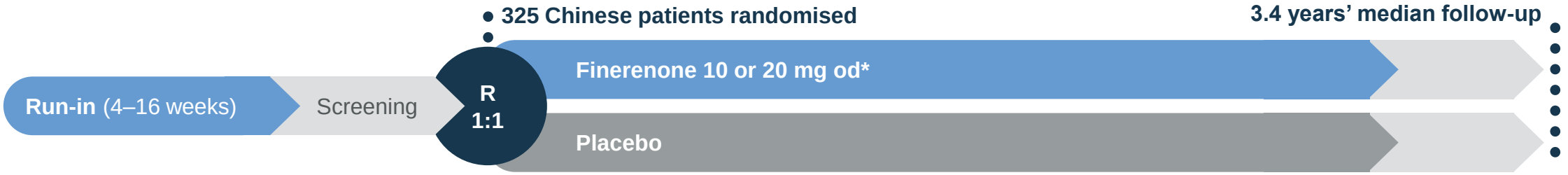
Finerenone is a selective nonsteroidal mineralocorticoid receptor antagonist shown to **delay CKD progression and reduce the risk of CV events** in the **phase III randomised clinical trials FIDELIO-DKD and FIGARO-DKD**[3,4]

Objective: This **FIGARO-DKD subgroup analysis** explored the **cardiovascular and kidney benefits of finerenone** in the **Chinese subgroup**

CKD, chronic kidney disease; CV, cardiovascular; T2D, type 2 diabetes

1. Wang L, *et al. JAMA Intern Med* 2023;183:298–310; 2. Khoo CM, *et al. Diabetes Obes Metab* 2021 23:299–317; 3. Bakris GL, *et al.* N Engl J Med. 2020;383:2219–2229; 4. Pitt B, *et al. N Engl J Med.* 2021;385:2252–2263

FIGARO-DKD was a randomised phase III trial of finerenone versus placebo in patients with early to middle stage CKD in T2D[1]



Key inclusion criteria

Aged ≥18 years with T2D

On max. tolerated dose of ACEi or ARB for ≥4 weeks

UACR 30–<300 mg/g and eGFR 25−90 ml/min/1.73 m^2 or UACR 300−5000 mg/g and eGFR ≥60 ml/min/1.73 m^2

Serum [K$^+$] ≤4.8 mmol/l at run-in and screening

Key exclusion criteria

HFrEF with NYHA Class II–IV

Uncontrolled arterial hypertension#

HbA1c >12%

Other kidney disease‡

Key endpoints

CV composite

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

Kidney composite

Time to kidney failure, sustained ≥40%/≥57% decrease in eGFR ≥4 weeks from baseline, or renal death

Albuminuria categories[2] (mg albumin/g creatinine)

GFR categories (ml/min/1.73 m^2)	A1 Normal to mildly increased (0–29)	A2 Moderately increased (30–299)	A3 Severely increased (≥300–≤5000)
G1 ≥90			
G2 60–89			
G3a 45–59			
G3b 30–44			
G4 15–29			
G5 <15			

*10 mg if screening eGFR <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; a decrease in the dose from 20 to 10 mg od was allowed any time after the initiation of finerenone or placebo; #mean sitting SBP ≥170 mmHg or mean sitting DBP ≥110 mmHg at the run-in visit, or mean sitting SBP ≥160 mmHg or mean sitting DBP ≥100 mmHg at the screening visit; ‡known significant nondiabetic kidney disease, including clinically relevant renal artery stenosis

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; CV, cardiovascular; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; HbA1c, glycated haemoglobin; HFrEF, heart failure with reduced ejection fraction; HHF, hospitalisation for heart failure; [K$^+$], potassium concentration; MI, myocardial infarction; NYHA, New York Heart Association; od, once daily; R, randomisation; SBP, systolic blood pressure; T2D, type 2 diabetes; UACR, urine albumin-creatinine ratio

1. Pitt B, *et al. N Engl J Med* 2021; 85:2252–2263; 2. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int* 2013;3:1–150

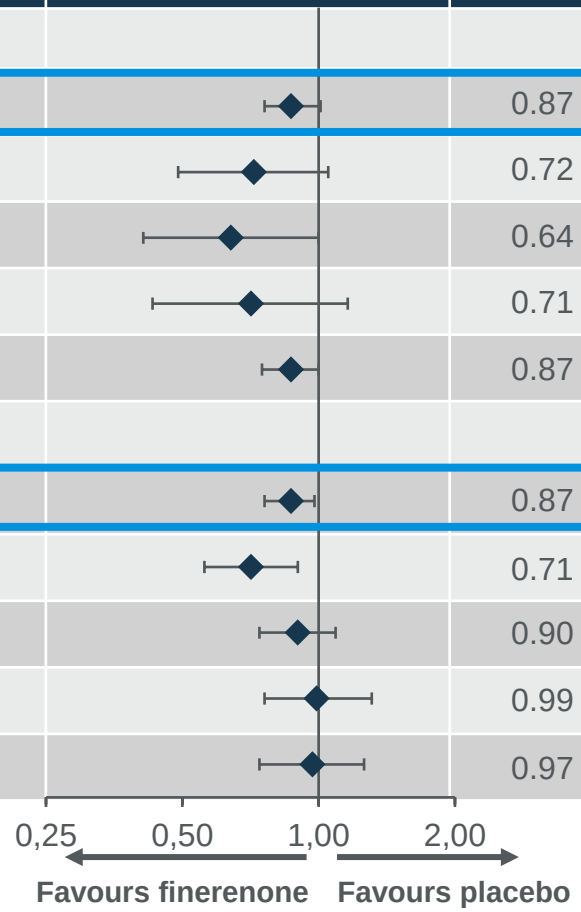
Chinese patients baseline characteristics

	Chinese subgroup	
Characteristic*	**Finerenone (N=162)**	**Placebo (N=163)**
Age, year, mean ± SD	60.62±10.20	56.98±11.42
Gender, female, n (%)	42 (25.9)	34 (20.9)
BMI, kg/m^2, mean ± SD	26.51±3.11	26.67±3.35
Duration of diabetes, years, mean ± SD	13.34±6.72	12.65±7.06
HbA1c, %, mean ± SD	7.53±1.41	7.53±1.28
Serum potassium, mmol/L, arithmetic mean ± SD	4.19±0.43	4.20±0.37
eGFR, ml/min/1.73 m^2, arithmetic mean ± SD	75.40±18.32	77.50±18.95
eGFR, ml/min/1.73m^2, n (%)		
<25	0 (0)	0 (0)
25 to <45	10 (6.2)	6 (3.7)
45 to <60	23 (14.2)	22 (13.5)
≥60	129 (79.6)	135 (82.8)
UACR, mg/g, median (Q1–Q3)	676 (320–1339)	779 (303–1614)
UACR, mg/g, n (%)		
<30	3 (1.9)	2 (1.2)
30–<300	35 (21.6)	38 (23.3)
≥300	124 (76.5)	123 (75.5)

*Values are n (%) or mean ± SD unless otherwise stated.
eGFR, estimated glomerular filtration rate; HbA1c, glycated haemoglobin; [K+], potassium concentration; Q, quartile; SBP, systolic blood pressure; UACR, urine albumin-to-creatinine ratio

In FIGARO-DKD, finerenone demonstrated kidney and heart benefits[1]

Outcome	Finerenone		Placebo			
	n (%)	n per 100 PY	n (%)	n per 100 PY	HR (95% CI)	p-value
Total population (N=7352)						
Kidney composite outcome	350 (9.5)	3.15	395 (10.8)	3.58	0.87 (0.76–1.01)	0.0689
Kidney failure	46 (1.2)	0.40	62 (1.7)	0.54	0.72 (0.49–1.05)	0.0889
ESKD	32 (0.9)	0.26	49 (1.3)	0.40	0.64 (0.41–1.00)	0.0458
eGFR <15 ml/min/1.73m^2	28 (0.8)	0.24	38 (1.0)	0.33	0.71 (0.43–1.16)	0.1711
≥40% decrease in eGFR from baseline	338 (9.2)	3.04	385 (10.5)	3.49	0.87 (0.75–1.00)	0.0526
Renal death	0 (0)	-	2 (<0.1)	-	-	-
CV composite outcome	458 (12.4)	3.87	519 (14.2)	4.45	0.87 (0.76–0.98)	0.0264
HHF	117 (3.2)	0.96	163 (4.4)	1.36	0.71 (0.56–0.90)	0.0043
CV death	194 (5.3)	1.56	214 (5.8)	1.74	0.90 (0.74–1.09)	0.2742
Nonfatal MI	103 (2.8)	0.85	102 (2.8)	0.85	0.99 (0.76–1.31)	0.9628
Nonfatal stroke	108 (2.9)	0.89	111 (3.0)	0.92	0.97 (0.74–1.26)	0.7932

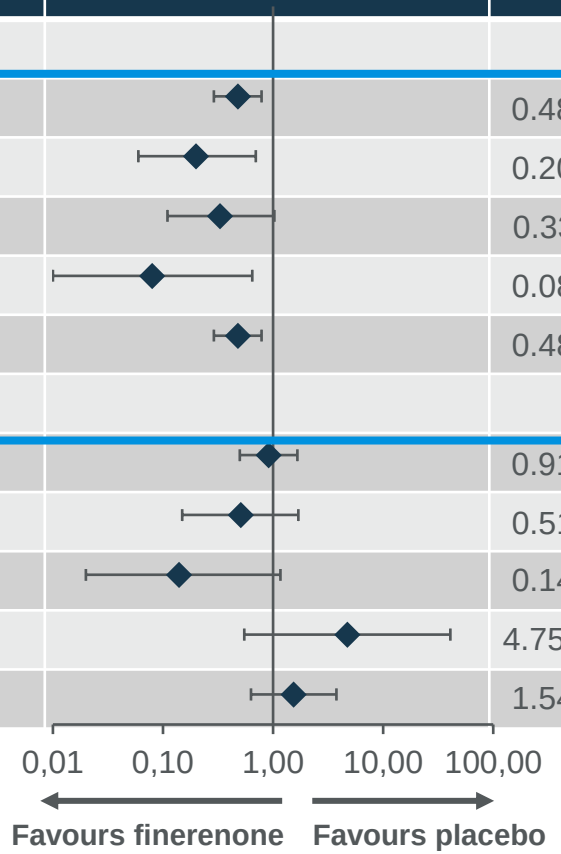


1. Pitt B, *et al. N Engl J Med* 2021; 85:2252–2263

CI, confidence interval; CV, cardiovascular; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HHF, hospitalisation for heart failure; HR, hazard ratio; MI, myocardial infarction; PY, patient-year

In the Chinese subgroup, finerenone demonstrated significant kidney benefits and numerically reduced CV outcomes

Outcome	Finerenone		Placebo				
	n (%)	n per 100 PY	n (%)	n per 100 PY		HR (95% CI)	p-value
Chinese subgroup (N=325)							
Kidney composite outcome	25 (15.4)	5.44	46 (28.2)	10.66		0.48 (0.29–0.79)	0.0029
Kidney failure	3 (1.9)	0.62	15 (9.2)	3.22		0.20 (0.06–0.70)	0.0050
ESKD	4 (2.5)	0.78	12 (7.4)	2.39		0.33 (0.11–1.03)	0.0457
eGFR <15 ml/min/1.73m^2	1 (0.6)	0.21	12 (7.4)	2.58		0.08 (0.01–0.65)	0.0025
≥40% decrease in eGFR from baseline	25 (15.4)	5.44	46 (28.2)	10.66		0.48 (0.29–0.79)	0.0029
Renal death	0 (0)	-	0 (0)	-		-	-
CV composite outcome	21 (13.0)	4.36	22 (13.5)	4.52		0.91 (0.50–1.67)	0.7660
HHF	4 (2.5)	0.79	8 (4.9)	1.61		0.51 (0.15–1.70)	0.2649
CV death	1 (0.6)	0.19	7 (4.3)	1.36		0.14 (0.02–1.17)	0.0346
Nonfatal MI	6 (3.7)	1.19	1 (0.6)	0.20		4.75 (0.55–40.75)	0.1165
Nonfatal stroke	12 (7.4)	2.44	8 (4.9)	1.60		1.54 (0.63–3.77)	0.3441

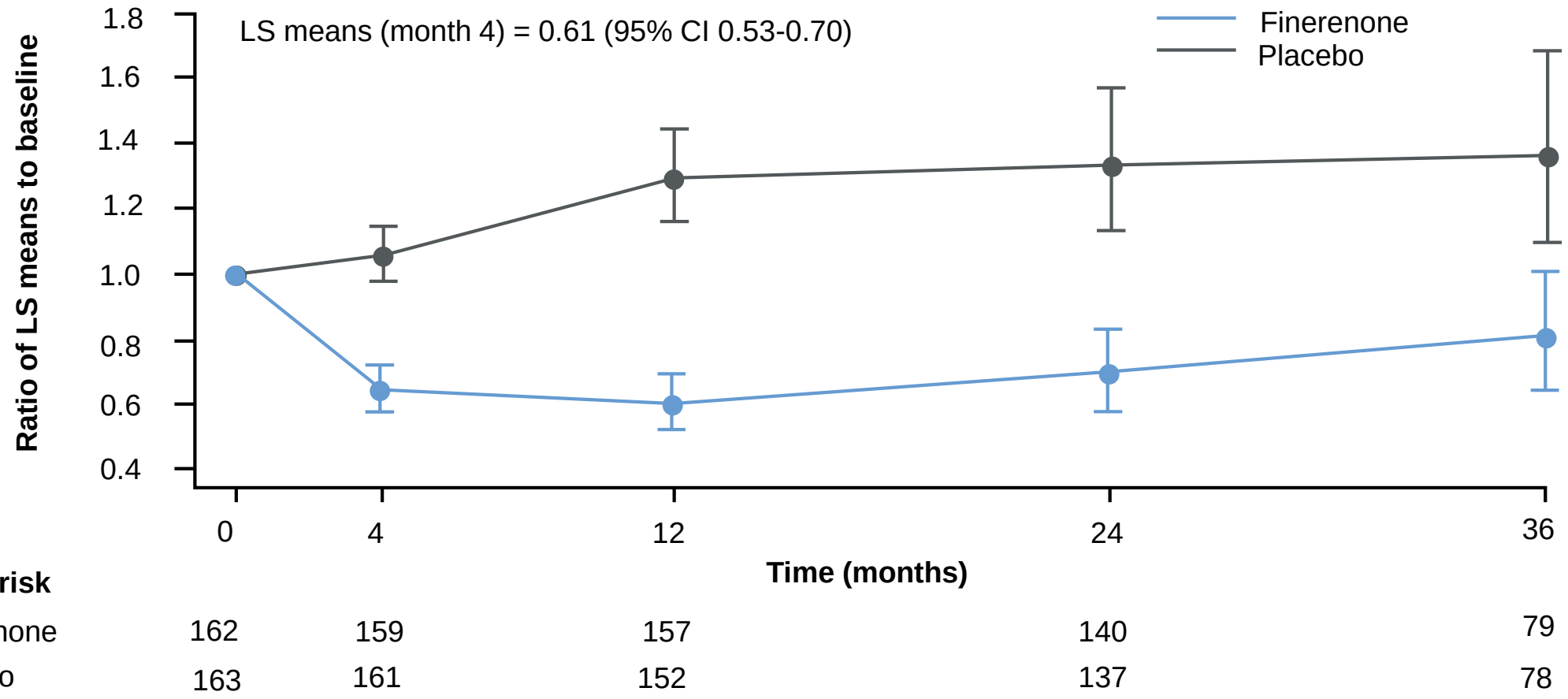


NNT = 7 (95% CI, 4–22) at **Month 36***
for ≥40% eGFR kidney composite endpoint

*Median treatment time was ~36 months in the Chinese subgroup

CI, confidence interval; CV, cardiovascular; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HHF, hospitalisation for heart failure; HR, hazard ratio; MI, myocardial infarction; PY, patient-year

In the Chinese subgroup, reduction in UACR from baseline at month 4 was significant and was maintained over the 3 years duration of the study



No. at risk

Finerenone	162	159	157	140	79
Placebo	163	161	152	137	78

The LS means and 95% CI were derived from a mixed model that takes treatment group, region, screening eGFR category, screening albuminuria type, time, time to treatment*, log-transition baseline value that matches the screen-phase albuminuria type as factors, and logarithmic-transformed baseline value*time as covariate. Independent unstructured covariance patterns were estimated for each treatment group. This analysis excludes values after the date of ESRD. For reference, the LS means reduction in UACR at month 4 in the total FIGARO-DKD population was 0.68 (95% CI 0.65−0.70)[1]

CI, confidence interval; eGFR, estimated glomerular filtration rate; ESRD, end-stage kidney disease; LS, ratio of least-squares; UACR, urine-albumin protein ratio

1. Pitt B, *et al. N Engl J Med* 2021; 85:2252–2263

Finerenone safety profile in the Chinese subgroup was similar with the total population

	Chinese subgroup		Total population[1]	
n (%)	Finerenone N=162	Placebo N=162	Finerenone N=3683	Placebo N=3658
Any TEAE	159 (98.1)	157 (96.9)	3134 (85.1)	3129 (85.5)
Any TEAE leading to study drug discontinuation	8 (4.9)	5 (3.1)	207 (5.6)	183 (5.0)
Any severe TEAE	82 (50.6)	84 (51.9)	1158 (31.4)	1215 (33.2)
Any SAE leading to study drug discontinuation	3 (1.9)	4 (2.5)	70 (1.9)	76 (2.1)
AE with outcome death	2 (1.2)	1 (0.6)	78 (2.1)	86 (2.4)
Any TEAE due to hyperkalaemia	31 (19.1)	30 (18.5)	396 (10.8)	193 (5.3)
Causing hospitalisation	1 (0.6)	0 (0)	21 (0.6)	2 (<0.1)
Leading to permanent discontinuation of study drug	1 (0.6)	1 (0.6)	46 (1.2)	13 (0.4)
Any hyperkalaemia	28 (17.3)	26 (16.0)	335 (9.1)	161 (4.4)
Serious	-	-	25 (0.7)	4 (0.1)
Severe	1 (0.6)	1 (0.6)	20 (0.5)	4 (0.1)
Severe, serious	0	1 (0.6)	15 (0.4)	3 (<0.1)
Serum potassium* > 5.5 mmol/l	15/161 (9.3)	14/161 (8.7)	495/3677 (13.5)	233/3655 (6.4)

In the Chinese subgroup, hyperkalaemia occurrences were similar between finerenone and placebo.

* Footnote in speaker notes

1. Pitt B, *et al. N Engl J Med* 2021; 85:2252–2263

AE, adverse event; TEAE, treatment-emergent adverse event; SAE, serious adverse event

Conclusions

In Chinese patients with CKD stage 1–4 with moderate-to-severely elevated albuminuria (UACR ≥30 mg/g), well-controlled SBP and HbA1c, treated with optimised RAS blockade, finerenone treatment:

Significantly reduced the risk of the composite kidney outcome and its components compared with placebo

Numerically reduced CV events compared with placebo

Overall AEs and SAEs were balanced between treatment arms; investigator-reported hyperkalaemia occurred more frequently in both the placebo and finerenone arm, respectively compared with the total population but the relative ratio was not increased

AE, adverse event; CKD, chronic kidney disease; CV, cardiovascular; HbA1, hemoglobin A1c; RAS, renin-angiotensin system; SAE, serious adverse event; SBP, systolic blood pressure; UACR, urine albumin-to-creatinine ratio

Thank you

48 countries; 19,381 patients enrolled; 7437 patients randomised

Executive committee
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Independent data monitoring committee
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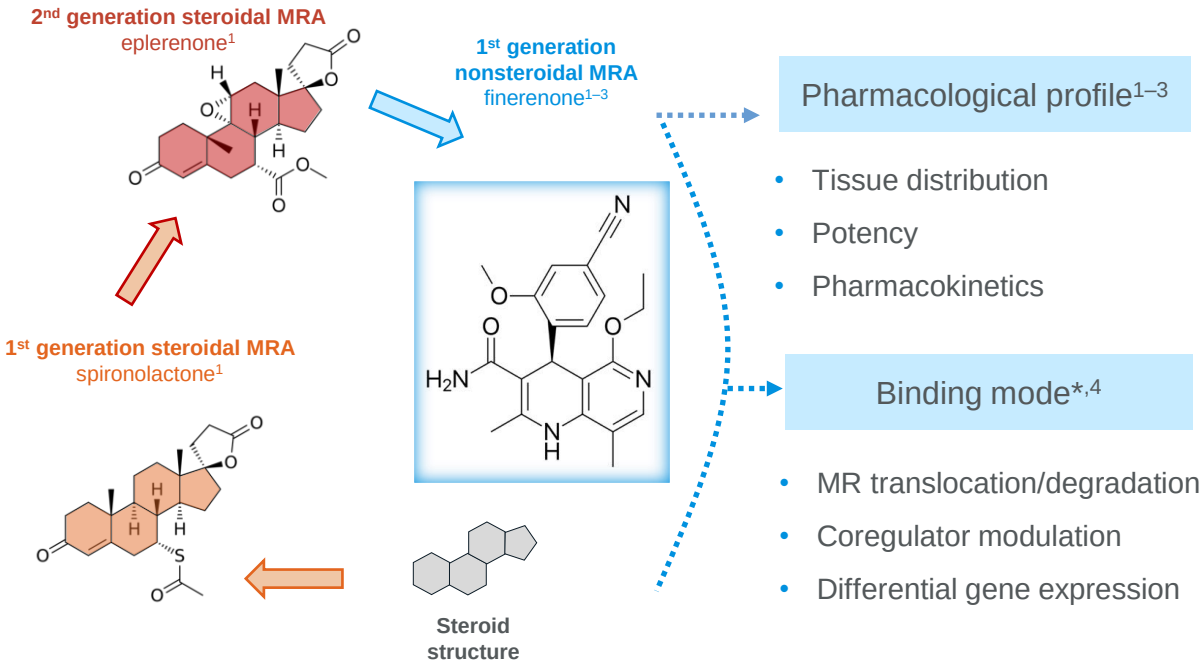
FIGARO-DKD

The FIGARO-DKD team would also like to thank all participating investigators, the centres, the patients and their families

Finerenone is a potent, highly selective, nonsteroidal MRA, with potential safety advantages over steroidal MRAs

- Differential modes of action between steroidal and the nonsteroidal MRAs[1–4]



- Key pharmacodynamic and pharmacokinetic differences[1,4]

	Spironolactone	Eplerenone	Finerenone
MRA class	Steroidal	Steroidal	Nonsteroidal
Potency to MR*	High	Low	High
Selectivity to MR*	Low	Medium	High
Metabolites*	Multiple, active	No active	No active
Tissue distribution*	Kidney ≫ heart (≥6-fold)	Kidney > heart (~3-fold)	Equivalent (1:1)

Finerenone is:

- More selective for MR receptor than spironolactone or eplerenone
- Highly potent
- More balanced heart:kidney distribution than steroidal MRAs

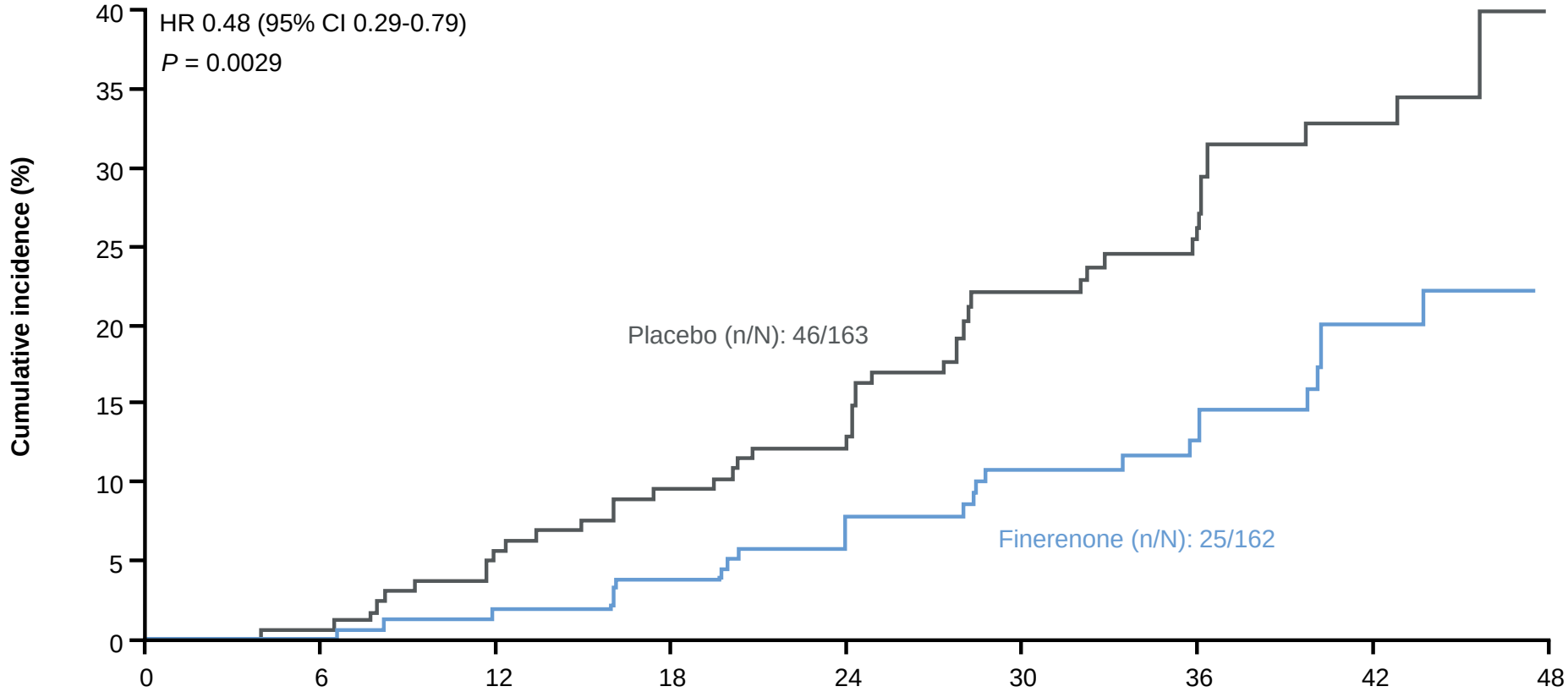
*Statements are based on preclinical data and are not supported by human studies
MR, mineralocorticoid receptor; MRA, mineralocorticoid receptor antagonist
1. Kolkhof P, *et al. Curr Opin Nephrol Hypertens* 2015;24:417–424; 2. Bärfacker L, *et al. ChemMedChem* 2012;7:1385–1403; 3. Amazit L, *et al. J Biol Chem* 2015;290:21876–21889;
4. Kolkhof P, *et al. Handb Exp Pharmacol* 2017;243:271–305

Chinese patients medication at baseline showed a high use of insulin but negligible use of SGLT-2is

	Chinese subgroup	
Medication use*	**Finerenone (N=162)**	**Placebo (N=163)**
ACEis	15 (9.3)	25 (15.3)
ARBs	145 (89.5)	138 (84.7)
Beta blockers	41 (25.3)	37 (22.7)
Diuretics	21 (13.0)	25 (15.3)
Statins	81 (50.0)	81 (49.7)
Potassium-lowering agents[#]	0 (0)	0 (0)
Glucose-lowering therapies	161 (99.4)	159 (97.5)
Insulin	122 (75.3)	118 (72.4)
GLP-1RAs	5 (3.1)	5 (3.1)
SGLT-2is	1 (0.6)	0 (0)

*Values are n (%); [#]Including sodium polystyrene sulfonate, calcium polystyrene sulfonate, and potassium-binding agents
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT-2i, sodium-glucose co-transporter-2 inhibitor

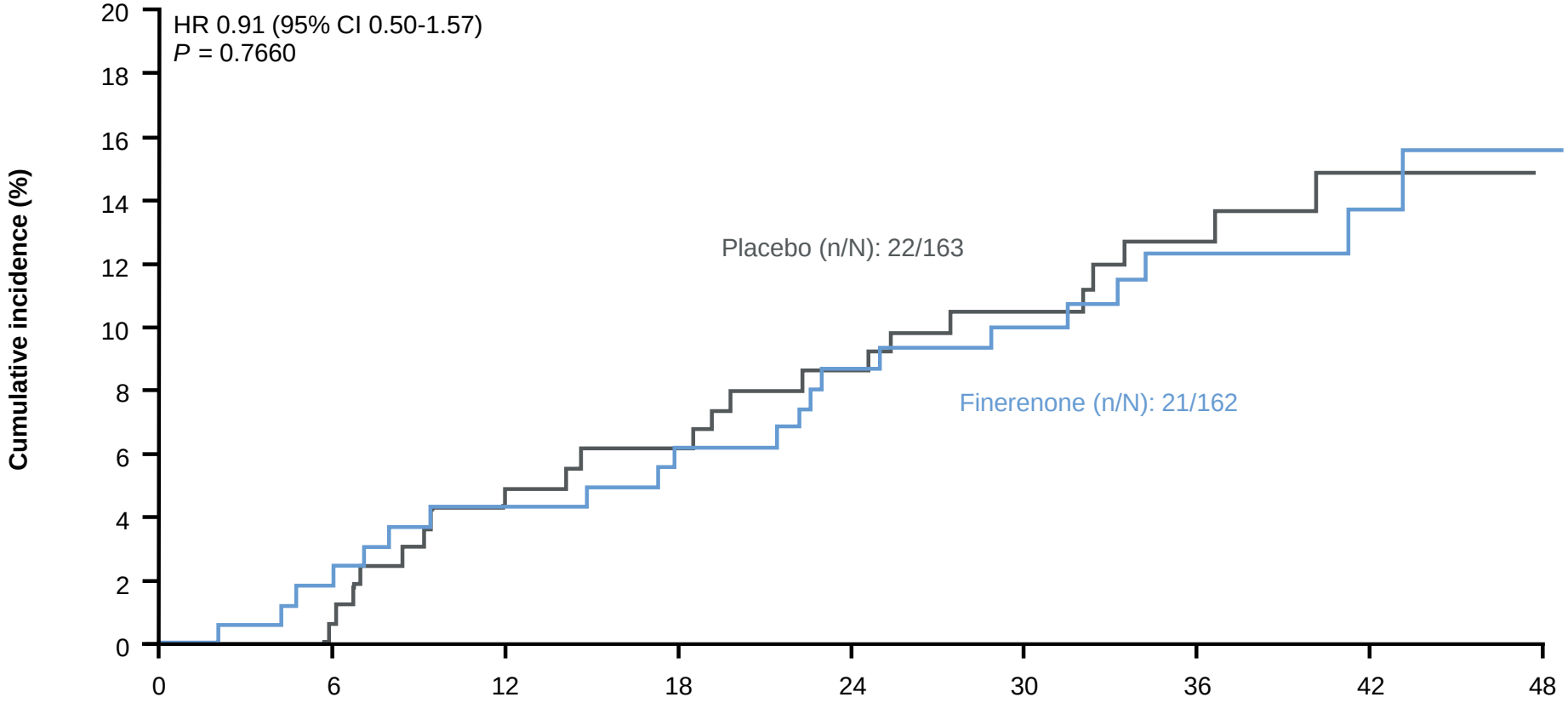
In the Chinese subgroup, finerenone significantly reduced the risk of the ≥40% kidney composite outcome: Time to kidney failure, sustained ≥40% decrease in eGFR from baseline, or renal death



No. at risk									
Finerenone	162	158	154	148	136	116	90	51	0
Placebo	163	159	148	139	130	104	77	44	0

CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio

In the Chinese subgroup, finerenone numerically reduced the risk of primary CV outcome: Time to first CV death, nonfatal stroke, nonfatal MI, and hospitalisation due to heart failure



No. at risk									
Finerenone	162	159	155	151	145	129	98	58	1
Placebo	163	162	155	152	148	133	101	58	0

CI, confidence interval; CV, cardiovascular; HR, hazard ratio; MI, myocardial infarction