Finerenone in heart failure with mildly reduced and preserved ejection fraction heart failure according to diabetes status: A pre-specified analysis of FINEARTS-HF

John McMurray

BHF Cardiovascular Research Centre, University of Glasgow & Queen Elizabeth University Hospital, Glasgow, Scotland, UK on behalf of the FINEARTS-HF committees and investigators

FINEARTS-HF: Background & introduction

- There are few proven treatments for patients with heart failure and mildly reduced or preserved ejection fraction (**HFmrEF or HFpEF**).
- Although steroidal mineralocorticoid receptor antagonists (MRAs) such as **spironolactone** reduce morbidity and mortality in patients with heart failure and reduced ejection fraction (HFrEF), their efficacy in HFmrEF/HFpEF is uncertain.
- **Finerenone** is a non-steroidal MRA with different physiochemical properties than steroidal MRAs and has been shown to reduce cardiovascular and kidney outcomes in two large trials in patients with T2D and CKD (FIGARO-DKD & FIDELIO-DKD).
- Therefore, we examined the efficacy and safety of finerenone in patients with HFmrEF/HFpEF, **with and without T2D**, in the **FINEARTS-HF** trial.
- Because FINEARTS-HF is the first large finerenone trial to include patients without T2D, we have analysed the effects of finerenone according to **baseline diabetes status**.
- Because spironolactone causes glucose intolerance, we also prespecified an analysis of **new-onset diabetes** in FINEARTS-HF.

FINEARTS-HF
FINerenone trial to investigate Efficacy and sAfety superioR to placebo in paTientS with Heart Failure

FINEARTS-HF: Trial design

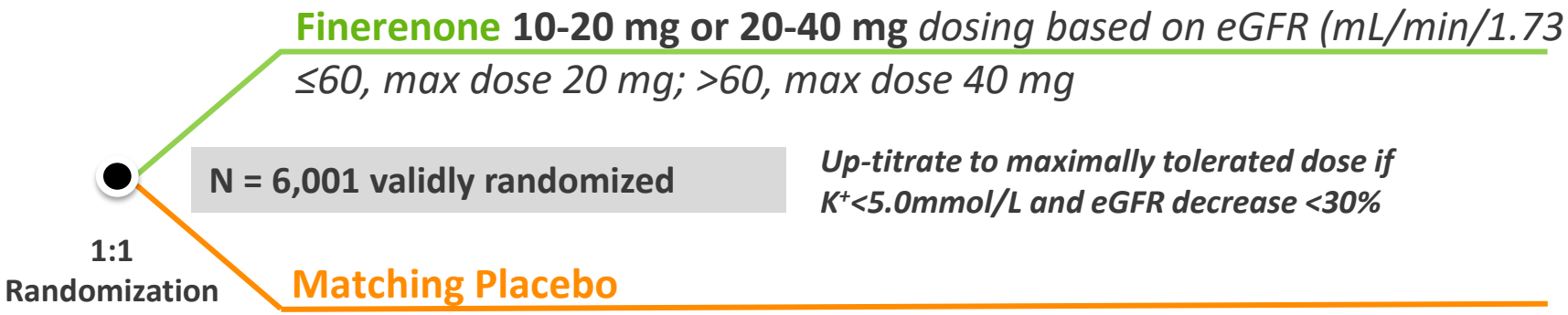
Randomized, double-blind, placebo-controlled trial testing the hypothesis that finerenone would reduce cardiovascular death and total worsening heart failure events in patients with heart failure and mildly reduced or preserved ejection fraction

Key inclusion criteria

- **Symptomatic HF (NYHA class II-V) with LVEF ≥40%**
- **Hospitalized, recently hospitalized, or ambulatory**
- **Elevated natriuretic peptide levels**
- **Structural heart disease (LA Enlargement or LVH)**
- **Diuretics in the 30 days prior to randomization**

Key exclusion criteria

- **Potassium >5.0 mmol/L; eGFR <25 mL/min/1.73 m²**
- **MRA use 30 days prior to randomization**
- **History of peripartum, chemotherapy induced, or infiltrative cardiomyopathy (e.g., amyloidosis)**
- **Alternative causes of signs or symptoms**



Visits: Month 1, then 3-monthly for first 12 months, 4-monthly visits thereafter with telephone contact in between

Trial endpoints

Primary Endpoint

- CV death and total HF events (hospitalizations/urgent visits)

Secondary Endpoints

- Total HF events
- KCCQ-TSS at 6,9, and 12 months
- NYHA class at 12 months
- Renal composite endpoint
- All-cause mortality

Solomon SD, McMurray JJV, Vaduganathan M, et al N Engl J Med. 2024 Sep 1. doi: 10.1056/NEJMoa2407107. Online ahead of print.

FINEARTS-HF
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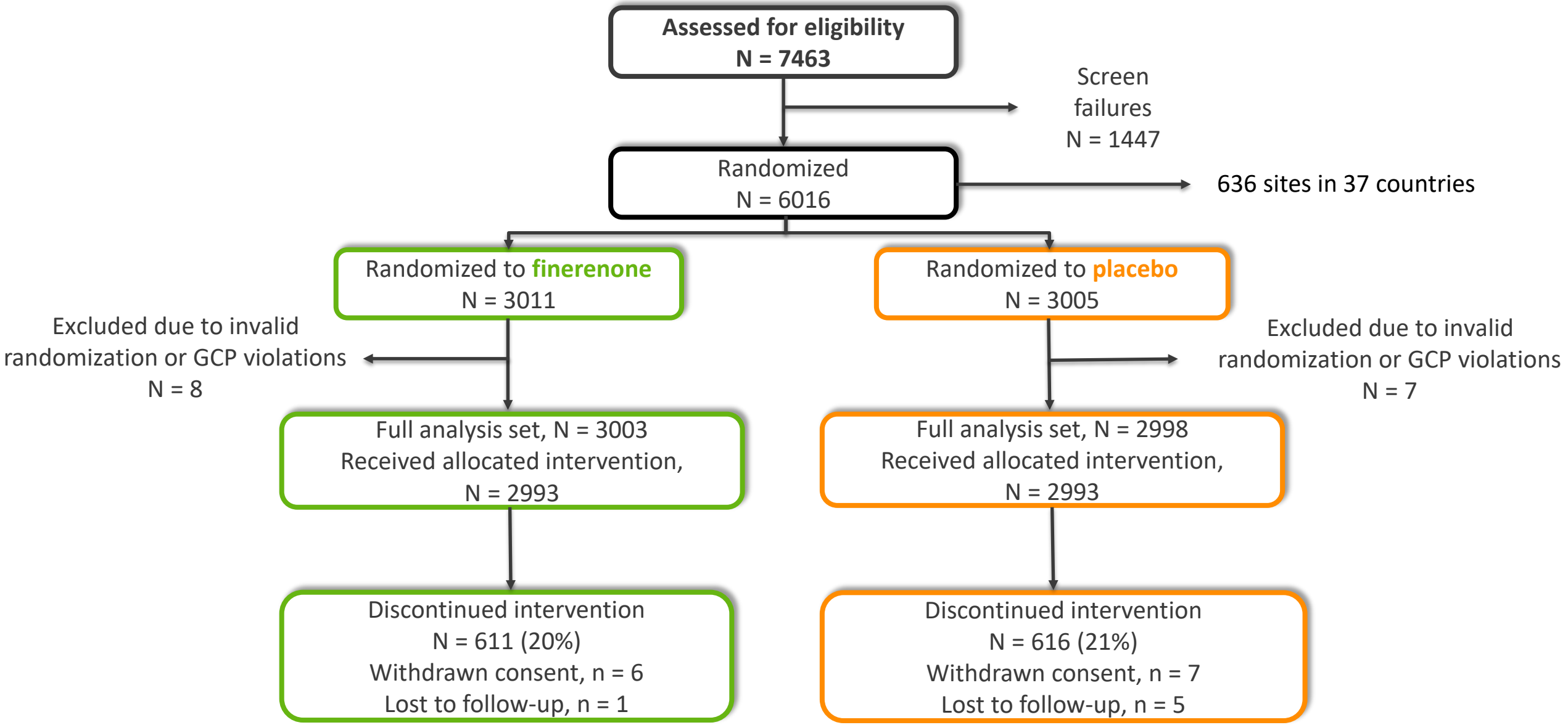
FINEARTS-HF: Patient flow



GCP, good clinical practice

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FINEARTS-HF: Presentation outline

- **Overall FINEARTS-HF results**
- **Effect of finerenone: type 2 versus no type 2 diabetes subgroup**
- **Effect of finerenone on the incidence of new diabetes**

FINEARTS-HF: Baseline characteristics

		Finerenone (N = 3003)	Placebo (N = 2998)
Age (yr)		72	72
Women (%)		45	46
Region (%)	Eastern Europe/Asia	44/16	44/16
	North America/Latin America	11/8	11/8
	Western Europe, Oceania and others	21	21
Systolic blood pressure (mmHg)		130	129
Body mass index (kg/m^2)		30	30
eGFR (mL/min/1.73m^2)		62	62
	eGFR <60 mL/min/1.73m^2 (%)	48	48
UACR (mg/g) [median]		18	19
Potassium (mmol/L)		4.4	4.4
LVEF mean (%)		53	53
NT-pro BNP (pg/mL) [median]		1052	1028
NYHA class II/III/IV (%)		69/30/1	69/30/1
Prior HF hospitalization (%)		60	61
Hypertension (%)		89	90
Type 2 diabetes (%)		41	41
Stroke (%)		12	12
Myocardial infarction (%)		26	25
Atrial fibrillation on ECG (%)		39	38

FINEARTS-HF: Medication at baseline

	Finerenone (N = 3003)	Placebo (N = 2998)
Beta-blocker	85	85
ACEI	36	36
ARB	35	35
ARNI	8.5	8.6
Loop diuretic	87	87
Thiazide diuretic	14	13
SGLT-2 inhibitor	**13**	**14**
Potassium supplementation	12	12

FINEARTS-HF
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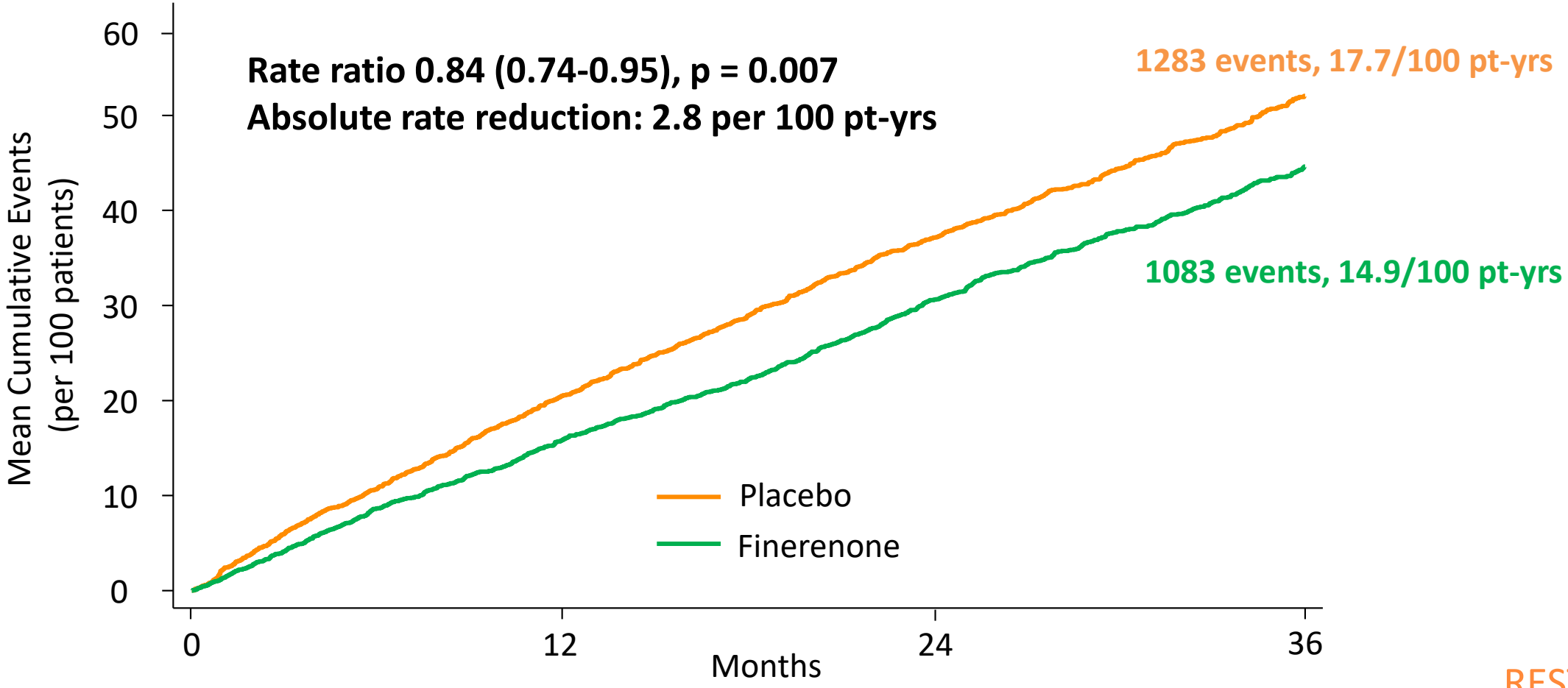
FINEARTS-HF: Primary endpoint

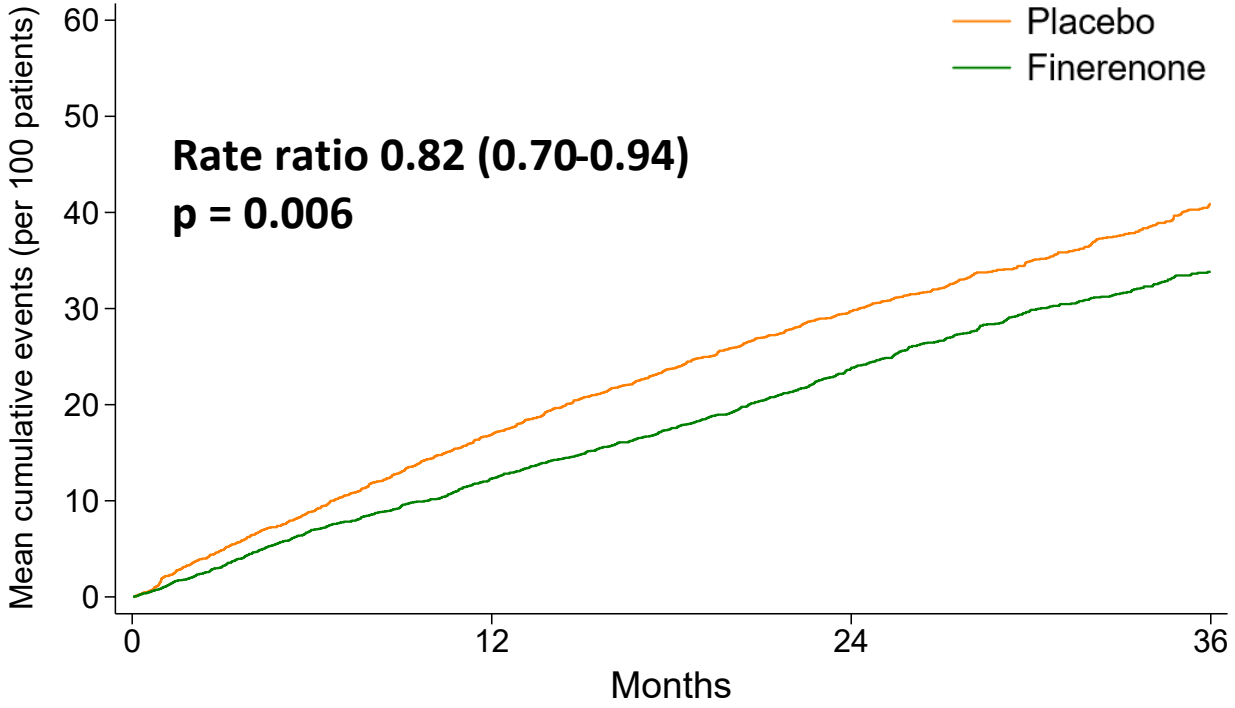
CV Death and total HF events

Median follow-up of 32 months

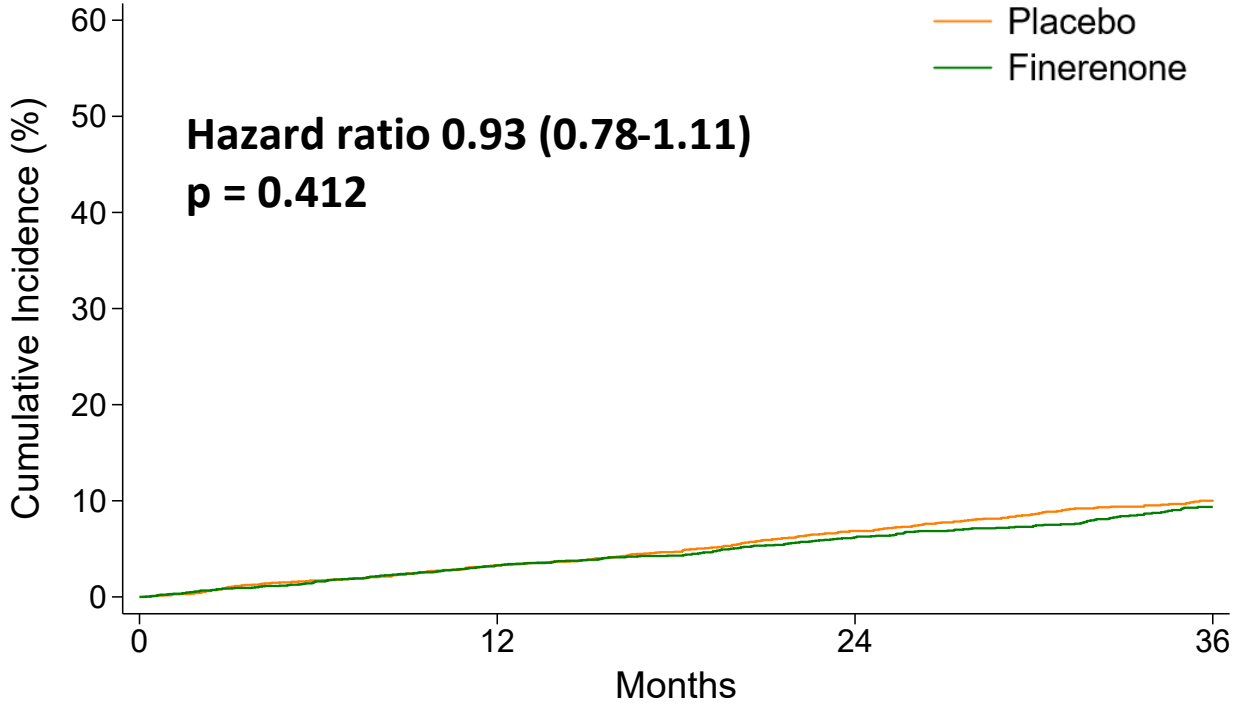


FINEARTS-HF: Components of primary endpoint

Total HF events



CV death



FINEARTS-HF: Prespecified safety and tolerability

Treatment emergent safety outcome	Finerenone (N=2993)	Placebo (N=2993)
Any Serious Adverse Event (SAE)	38.7%	40.5%
Serum creatinine ≥3.0 mg/dl	2.0%	1.2%
Serum potassium		
>5.5 mmol/l	14.3%	6.9 %
>6.0 mmol/l	3.0 %	1.4 %
<3.5 mmol/l	4.4 %	9.7 %
Investigator-reported hyperkalaemia	9.7%	4.2%
Leading to hospitalization	0.5%	0.2%
Leading to death	0%	0%
Systolic blood pressure <100 mmHg	18.5%	12.4%

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FINEARTS-HF: Baseline characteristics

	No diabetes N=3,547	Diabetes N=2,439	P-value
Age (years)	72	71	<0.001
Women (%)	48	**42**	<0.001
Geographic region (%)			0.002
Eastern Europe/Asia	44/17	44/16	
North America/Latin America	7/10	9/11	
Western Europe, Oceania and others	21	20	
Systolic blood pressure (mmHg)	129	130	<0.001
NT-proBNP (pg/mL), median	1069	1002	0.16
LVEF (%)	53	53	0.75
NYHA class II/III/IV (%)	70/29/<1	**67/32/1**	0.012
KCCQ-TSS points (out of 100)	68	**65**	<0.001
Hospitalization for HF (%)	59	**63**	0.002
Stroke (%)	14	14	0.71
Myocardial infarction (%)	22	**31**	<0.001
Hypertension (%)	86	**93**	<0.001
Atrial fibrillation/flutter on ECG (%)	42	**34**	<0.001

FINEARTS-HF: Baseline characteristics

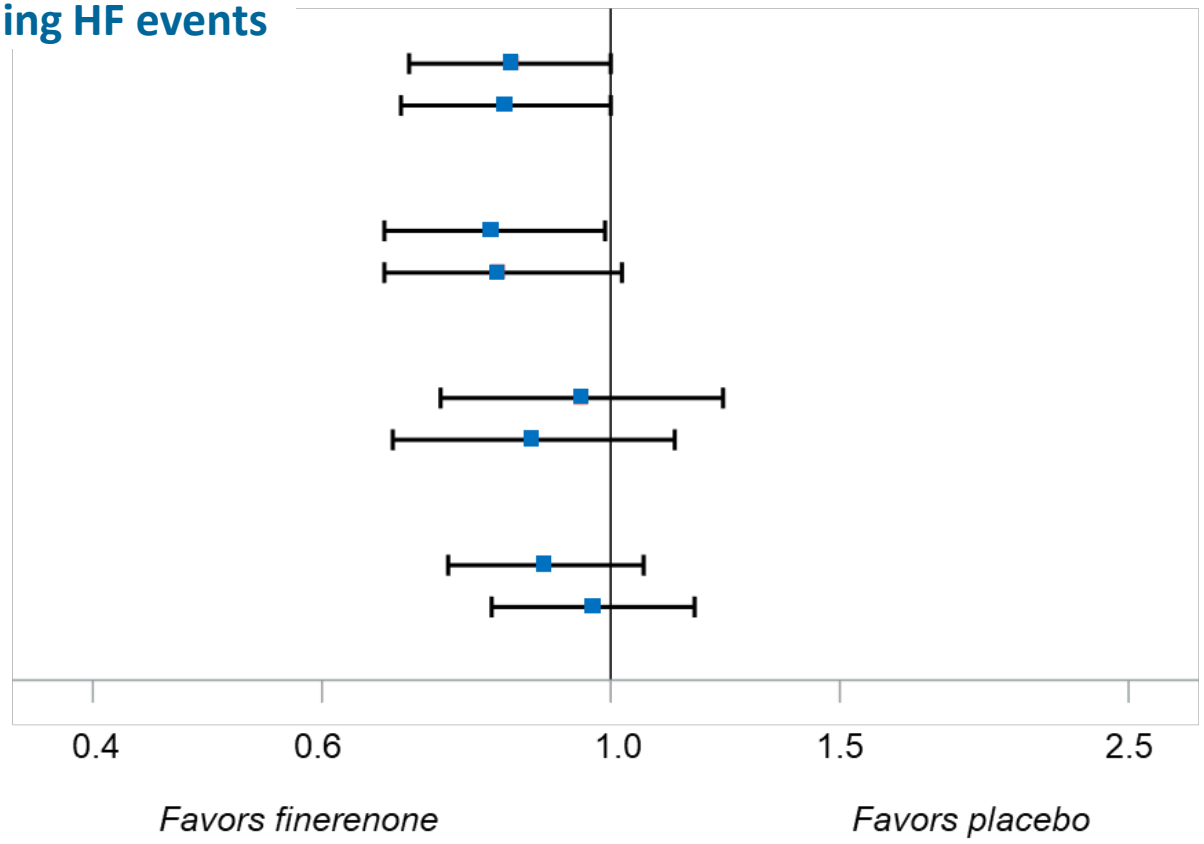
	No diabetes N=3,547	Diabetes N=2,439	P-value
Body mass index (Kg/m^2)	29	31	<0.001
Body mass index categories			<0.001
<18.5	1.4	0.6	
18.5-24.9	24	15	
25.0-29.9	35	30	
30-34.9	23	**30**	
≥35.0	16	**24**	
Haemoglobin A1c (%)	5.9	**7.2**	<0.001
eGFR (mL/min/1.73m^2)	63.6	**59.9**	<0.001
eGFR <60 mL/min/1.73m^2 (%)	45	**53**	<0.001
Urine albumin-to-creatinine ratio (mg/g), median	14	32	<0.001
Urine albumin-to-creatinine ratio, categories (%)			<0.001
<30	69	48	
30-299	26	**35**	
=>300	5	**17**	
Potassium (mmol/L)	4.4	4.4	<0.001

FINEARTS-HF: Baseline treatment

	No diabetes N=3,547	Diabetes N=2,439	P-value
Heart failure treatments, (%)			
ACEi	36	36	0.74
ARB	33	37	0.002
ARNI	8	9	0.71
Beta-blocker	84	86	0.053
SGLT2i	6	25	<0.001
Loop diuretic	87	88	0.033
Any diuretic	99	99	0.46
Digoxin	9	6	<0.001
Glycaemia treatments, (%)			
Insulin	0.1	28	<0.001
Biguanide	0.5	57	<0.001
Sulfonylurea	0	17	<0.001
DPP-4 inhibitor	0	18	<0.001
GLP-1 analogue	0.1	7	<0.001
Glitazone	0	1.3	<0.001
Glinide	0	1.6	<0.001
Alpha glucosidase inhibitor	0	2.5	<0.001

FINEARTS-HF: Key outcomes

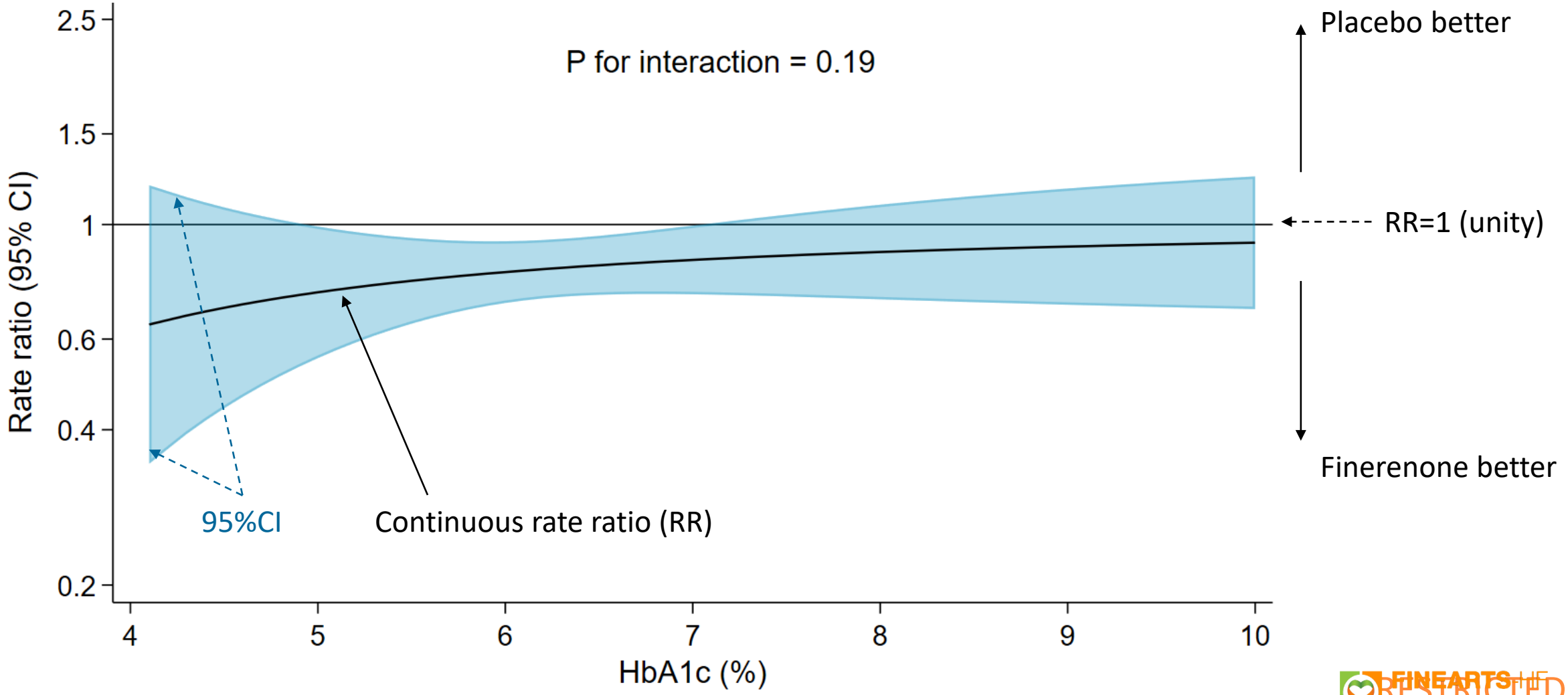
Consistent effect of finerenone irrespective of diabetes status



	HR/RR (95% CI)	P-value for Interaction
Cardiovascular death and total worsening HF events		0.91
No history of diabetes	0.84 (0.70-1.00)	
History of diabetes	0.83 (0.69-1.00)	
Total worsening HF events		1.00
No history of diabetes	0.81 (0.67-0.99)	
History of diabetes	0.82 (0.67-1.02)	
Cardiovascular death		0.64
No history of diabetes	0.95 (0.74-1.22)	
History of diabetes	0.87 (0.68-1.12)	
All-cause death		0.50
No history of diabetes	0.89 (0.75-1.06)	
History of diabetes	0.97 (0.81-1.16)	

FINEARTS-HF: Primary outcome according to HbA1c

Cardiovascular death and total worsening HF events



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- **Overall FINEARTS-HF results**
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- **Effect of finerenone on the incidence of new diabetes**

FINEARTS-HF: No diabetes at baseline

	Finerenone N=1,606	Placebo N=1,616
Age (years)	72	72
Women (%)	46	48
Geographic region (%)		
Eastern Europe/Asia	43/18	45/16
North America/Latin America	7/10	6/11
Western Europe, Oceania and others	21	22
Systolic blood pressure (mmHg)	129	129
NT-proBNP (pg/mL), median	1064	1069
LVEF (%)	53	53
NYHA class II/III/IV (%)	72/27/<1	71/29/<1
Hospitalization for HF (%)	58	59
Stroke (%)	13	14
Myocardial infarction (%)	23	21
Hypertension (%)	85	87
Atrial fibrillation/flutter on ECG (%)	42	41

FINEARTS-HF: No diabetes at baseline

	Finerenone N=1,606	Placebo N=1,616
Body mass index (Kg/m^2)	29	29
Body mass index, categories (%)		
<18.5	2	1
18.5-24.9	25	24
25.0-29.9	34	36
30-34.9	23	23
≥35.0	15	16
Haemoglobin A1c (%)	5.7	5.7
Pre-diabetes (%)	**62**	**61**
eGFR (mL/min/1.73m^2)	64	64
eGFR <60 mL/min/1.73m^2, (%)	44	44
Potassium, (mmol/L)	4.4	4.3
Urine albumin-to-creatinine ratio (mg/g), median	13.0	13.6
Urine albumin-to-creatinine ratio, categories (%)		
<30	70	69
30-299	26	26
=>300	4	5

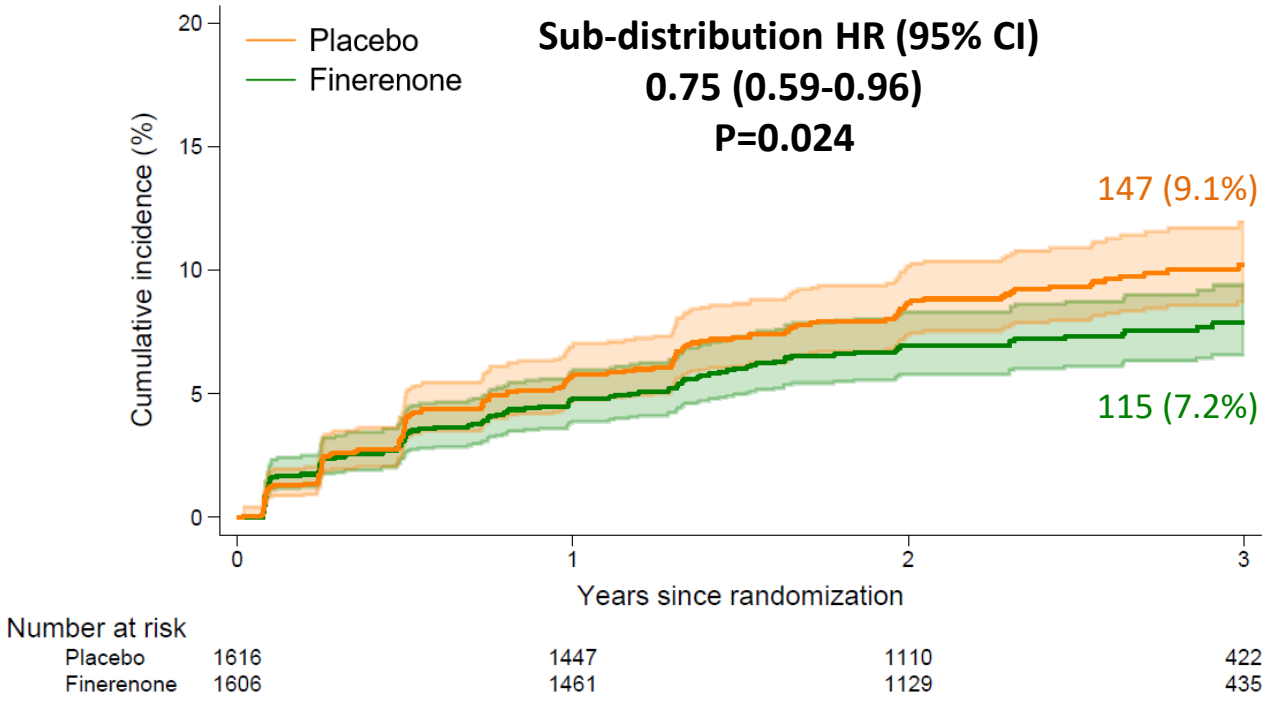
FINEARTS-HF: No diabetes at baseline

Drug therapy (%)	Finerenone N=1,606	Placebo N=1,616
ACEi	36	36
ARB	33	34
ARNI	9	8
Beta-blocker	83	84
SGLT2i	5	6
Loop diuretic	86	86
Any diuretic	99	99
Digoxin	9	8

FINEARTS-HF: Incidence of new diabetes

Significant reduction in new onset diabetes with finerenone

HbA1c measurement ≥6·5% on 2 consecutive follow-up visits or initiation of glucose-lowering drugs *excluding* SGLT2 inhibitors



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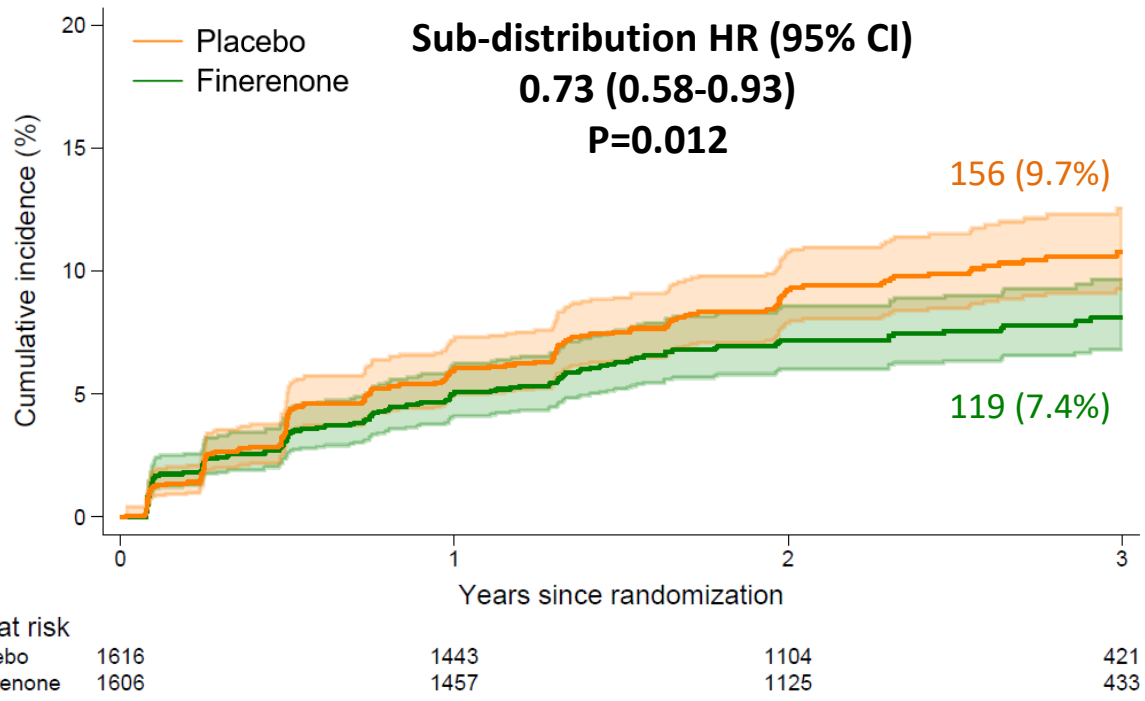
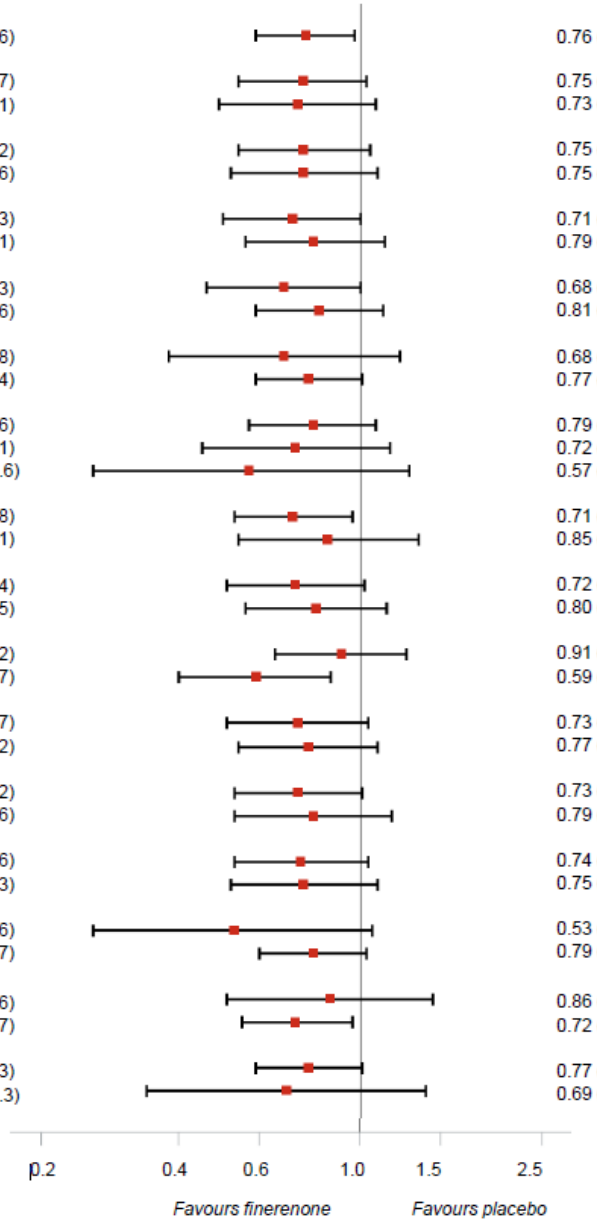


FINEARTS-HF: Incidence of new diabetes in subgroups

	n/N		Event rate per 100 person-years (95% CI)		Hazard ratio (95% CI)	P-value for interaction
	Finerenone	Placebo	Finerenone	Placebo		
Overall	115/1,6076	147/1,616	3.0 (2.5-3.6)	3.9 (3.3-4.6)	0.76 (0.59-0.97)	
Age, years						0.93
<74	69 / 817	88 / 799	3.5 (2.8-4.5)	4.6 (3.7-5.7)	0.75 (0.54-1.03)	
≥74	46 / 789	59 / 817	2.5 (1.9-3.3)	3.2 (2.5-4.1)	0.73 (0.49-1.08)	
Sex						0.97
Male	67 / 860	80 / 835	3.3 (2.6-4.2)	4.2 (3.4-5.2)	0.75 (0.54-1.05)	
Female	48 / 746	67 / 781	2.7 (2.0-3.6)	3.6 (2.9-4.6)	0.75 (0.52-1.09)	
BMI, kg/m²						0.72
<30	57 / 986	78 / 990	2.5 (1.9-3.2)	3.4 (2.7-4.3)	0.71 (0.50-1.00)	
≥30	58 / 617	69 / 622	3.9 (3.0-5.1)	4.8 (3.7-6.1)	0.79 (0.56-1.13)	
Waist, cm						0.59
≤Median	44 / 754	60 / 762	2.4 (1.8-3.3)	3.4 (2.6-4.3)	0.68 (0.46-1.00)	
>Median	70 / 840	87 / 843	3.5 (2.8-4.5)	4.5 (3.6-5.6)	0.81 (0.59-1.12)	
Glycaemic status						0.75
Normoglycaemia	22 / 615	30 / 628	1.4 (1.0-2.2)	1.9 (1.4-2.8)	0.68 (0.38-1.22)	
Pre-diabetes	93 / 991	117 / 988	4.1 (3.3-5.0)	5.3 (4.4-6.4)	0.77 (0.59-1.01)	
Smoking status						0.64
Never	70 / 996	91 / 1042	2.9 (2.3-3.7)	3.7 (3.0-4.6)	0.79 (0.57-1.08)	
Former	34 / 473	39 / 453	3.1 (2.2-4.4)	3.7 (2.7-5.1)	0.72 (0.45-1.16)	
Current	11 / 137	17 / 137	3.4 (1.8-6.1)	6.5 (4.0-10.6)	0.57 (0.26-1.28)	
NYHA class						0.56
II	80 / 1157	107 / 1140	2.9 (2.3-3.6)	4.0 (3.3-4.8)	0.71 (0.53-0.96)	
III/IV	35 / 448	40 / 476	3.5 (2.5-4.9)	3.7 (2.7-5.1)	0.85 (0.54-1.34)	
KCCQ-TSS						0.68
≤Median	56 / 768	82 / 854	3.1 (2.4-4.1)	4.3 (3.5-5.4)	0.72 (0.51-1.02)	
>Median	59 / 837	65 / 758	2.9 (2.3-3.8)	3.5 (2.8-4.5)	0.80 (0.56-1.14)	
LVEF, %						0.076
≤Median	69 / 797	77 / 816	3.7 (2.9-4.7)	4.1 (3.3-5.2)	0.91 (0.65-1.26)	
>Median	46 / 806	70 / 799	2.4 (1.8-3.2)	3.7 (2.9-4.7)	0.59 (0.40-0.86)	
NT-proBNP						0.93
≤Median	58 / 784	70 / 784	3.0 (2.3-3.9)	3.7 (2.9-4.7)	0.73 (0.51-1.04)	
>Median	55 / 781	74 / 787	3.1 (2.3-4.0)	4.2 (3.3-5.2)	0.77 (0.54-1.09)	
eGFR, ml/min/1.73 m²						0.81
≥60	68 / 906	90 / 900	3.1 (2.4-4.0)	4.2 (3.4-5.2)	0.73 (0.53-1.01)	
<60	47 / 700	57 / 716	2.9 (2.2-3.9)	3.5 (2.7-4.6)	0.79 (0.53-1.17)	
Potassium, mmol/L						0.91
≤Median	62 / 792	84 / 817	3.3 (2.6-4.3)	4.5 (3.6-5.6)	0.74 (0.53-1.04)	
>Median	53 / 814	63 / 799	2.7 (2.1-3.6)	3.4 (2.6-4.3)	0.75 (0.52-1.09)	
Beta-blocker use at baseline						0.42
No	13 / 268	21 / 259	2.1 (1.2-3.6)	3.6 (2.4-5.6)	0.53 (0.26-1.06)	
Yes	102 / 1338	126 / 1357	3.2 (2.6-3.9)	4.0 (3.3-4.7)	0.79 (0.60-1.03)	
ACEi/ARB/ARNI use at baseline						0.60
No	27 / 369	31 / 353	3.1 (2.1-4.6)	3.9 (2.8-5.6)	0.86 (0.51-1.44)	
Yes	88 / 1237	116 / 1263	3.0 (2.4-3.7)	3.9 (3.3-4.7)	0.72 (0.55-0.96)	
Digoxin						0.60
No	100 / 1463	124 / 1487	2.9 (2.4-3.5)	3.6 (3.0-4.3)	0.77 (0.59-1.01)	
Yes	15 / 143	23 / 129	4.5 (2.7-7.6)	8.0 (5.3-12.3)	0.69 (0.34-1.39)	



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Sex						0.97
Male	67 / 860	80 / 835	3.3 (2.6-4.2)	4.2 (3.4-5.2)	0.75 (0.54-1.05)	
Female	48 / 746	67 / 781	2.7 (2.0-3.6)	3.6 (2.9-4.6)	0.75 (0.52-1.09)	
BMI, Kg/m²						0.72
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Glycaemic status						0.75
Normoglycaemia	22 / 615	30 / 628	1.4 (1.0-2.2)	1.9 (1.4-2.8)	0.68 (0.38-1.22)	
Pre-diabetes	93 / 991	117 / 988	4.1 (3.3-5.0)	5.3 (4.4-6.4)	0.77 (0.59-1.01)	
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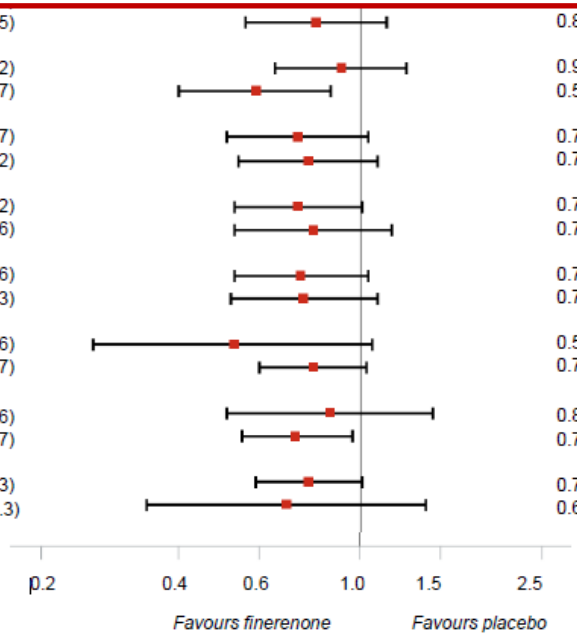
<60	47 / 700	57 / 716	2.9 (2.2-3.9)	3.5 (2.7-4.6)	0.79 (0.53-1.17)	
Potassium, mmol/L						0.91
≤Median	62 / 792	84 / 817	3.3 (2.6-4.3)	4.5 (3.6-5.6)	0.74 (0.53-1.04)	
>Median	53 / 814	63 / 799	2.7 (2.1-3.6)	3.4 (2.6-4.3)	0.75 (0.52-1.09)	
Beta-blocker use at baseline						0.42
No	13 / 268	21 / 259	2.1 (1.2-3.6)	3.6 (2.4-5.6)	0.53 (0.26-1.06)	
Yes	102 / 1338	126 / 1357	3.2 (2.6-3.9)	4.0 (3.3-4.7)	0.79 (0.60-1.03)	
ACEi/ARB/ARNI use at baseline						0.60
No	27 / 369	31 / 353	3.1 (2.1-4.6)	3.9 (2.8-5.6)	0.86 (0.51-1.44)	
Yes	88 / 1237	116 / 1263	3.0 (2.4-3.7)	3.9 (3.3-4.7)	0.72 (0.55-0.96)	
Digoxin						0.60
No	100 / 1463	124 / 1487	2.9 (2.4-3.5)	3.6 (3.0-4.3)	0.77 (0.59-1.01)	
Yes	15 / 143	23 / 129	4.5 (2.7-7.6)	8.0 (5.3-12.3)	0.69 (0.34-1.39)	



FINEARTS-HF: Summary and conclusions

- Among patients with heart failure and a mildly reduced or preserved ejection fraction, finerenone reduced the risk of the primary composite outcome of cardiovascular death and total heart failure events and reduced total heart failure events.
- These findings were consistent across prespecified subgroups, **including people with and without type 2 diabetes at baseline**.
- Hyperkalaemia was more common, and hypokalaemia less common, in those randomised to finerenone (versus placebo).
- **Finerenone reduced the incidence of new diabetes** by about a quarter in patients with heart failure with mildly reduced or preserved ejection fraction.