

Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction: The FINEARTS-HF Trial

Scott D. Solomon, MD

Brigham and Women's Hospital

Harvard Medical School

on behalf of the FINEARTS-HF Investigators



Rationale

- Despite the availability of several therapeutic options in heart failure with mildly reduced or preserved ejection fraction (HFmrEF or HFpEF), including SGLT2 inhibitors, there remains a high unmet need in this population^{1,2,3}.
- Steroidal mineralocorticoid receptor antagonists (spironolactone, eplerenone) reduce morbidity and mortality in patients with heart failure and reduced ejection fraction; their efficacy in those with HFmrEF or HFpEF has not been established^{4,5}.
- While spironolactone did not reduce the primary endpoint in the TOPCAT trial, post hoc analyses revealed that a substantial proportion of enrolled patients outside of the Americas may not have had heart failure and probably did not take investigational therapy^{6,7}. MRAs are not currently recommended in ESC Guidelines for HFpEF.
- Finerenone is a non-steroidal MRA which, compared with steroidal MRAs, is more selective for the MR receptor, has a shorter half-life, and has a more balanced distribution between the heart and the kidney

1. Solomon et al, NEJM 2019 2. Anker et al. NEJM 2021 3. Solomon et al NEJM 2022 4. Pitt et al. NEJM 1999; 5. Zannad et. al. NEJM 2011 6. Pitt et al. NEJM 2013; 7. Pfeffer et al. Circulation. 2013

FINEARTS-HF Study 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 \geq 40%
- Hospitalized, recently hospitalized, or ambulatory
- Elevated natriuretic peptide levels
- Structural heart disease (LA Enlargement or LVH)
- Diuretics in the 30d prior to randomization

Key Exclusion Criteria

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

Finerenone 10, 20 or 20, 40 mg dosing based on eGFR: \leq 60 max dose 20 mg, $>$ 60, max dose 40 mg

N = 6,001 validly randomized

Uptitrate to maximally tolerated dose if $K^+ <$ 5.0 mmol/L and eGFR decrease $<$ 30%

1:1

Randomization

Matching Placebo

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

Study Endpoints

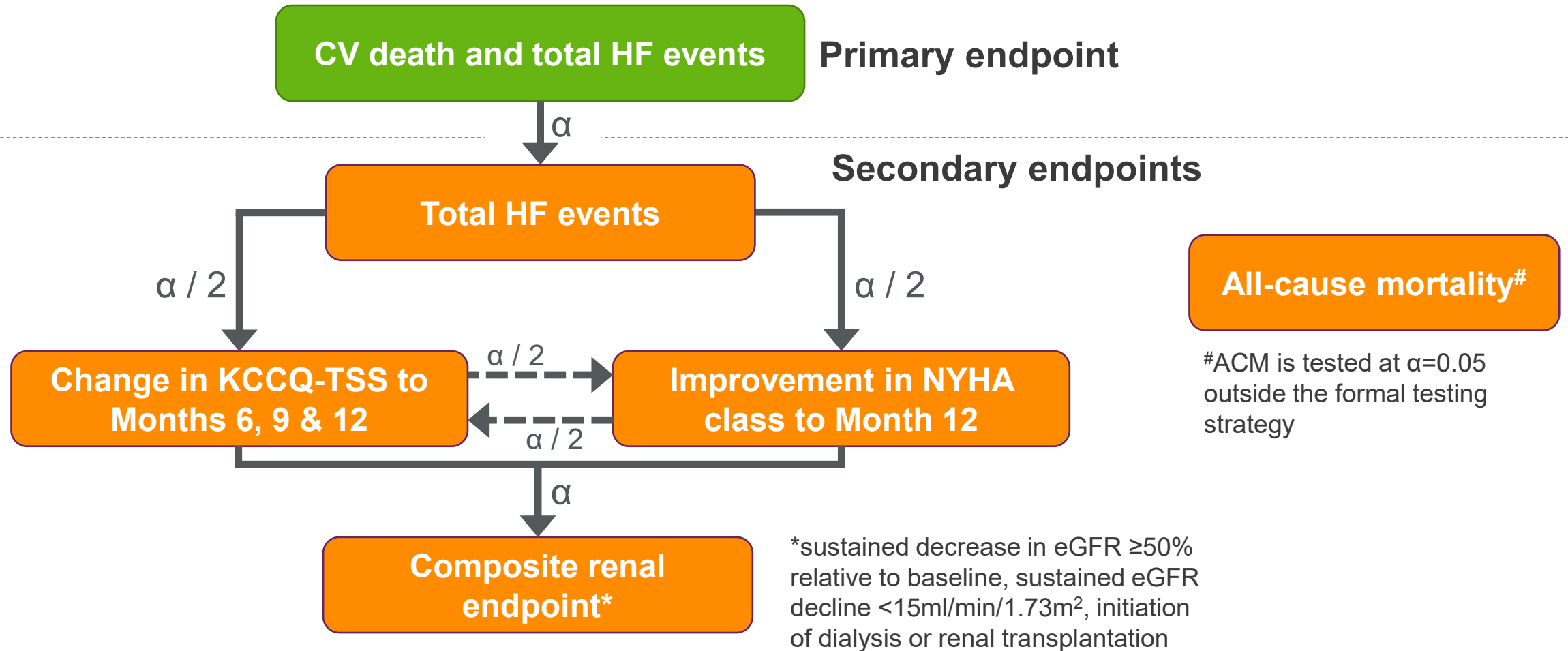
Primary Endpoint

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

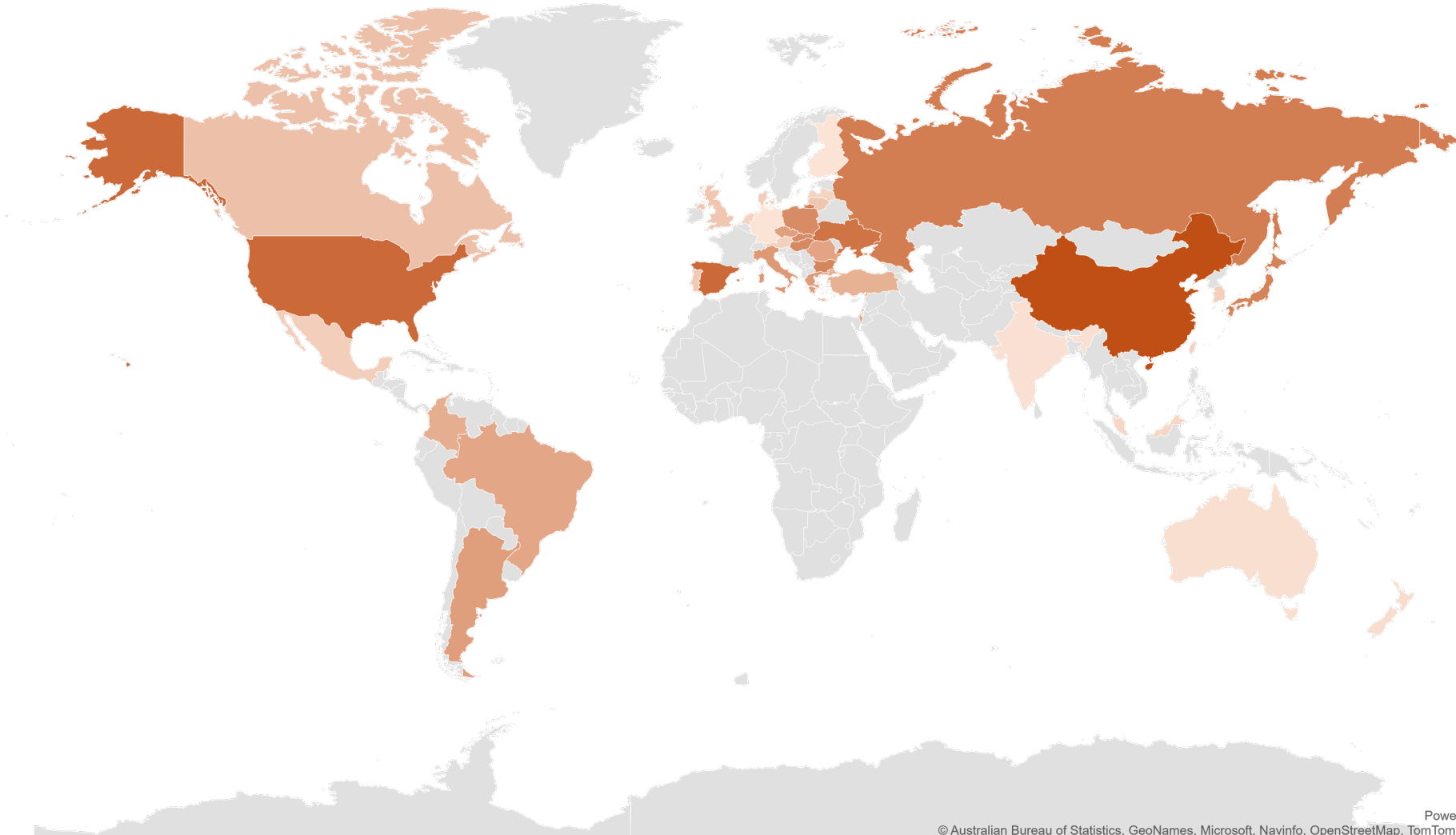
Secondary Endpoints

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

Endpoints and Analysis Plan



Global randomization across 635 sites in 37 countries

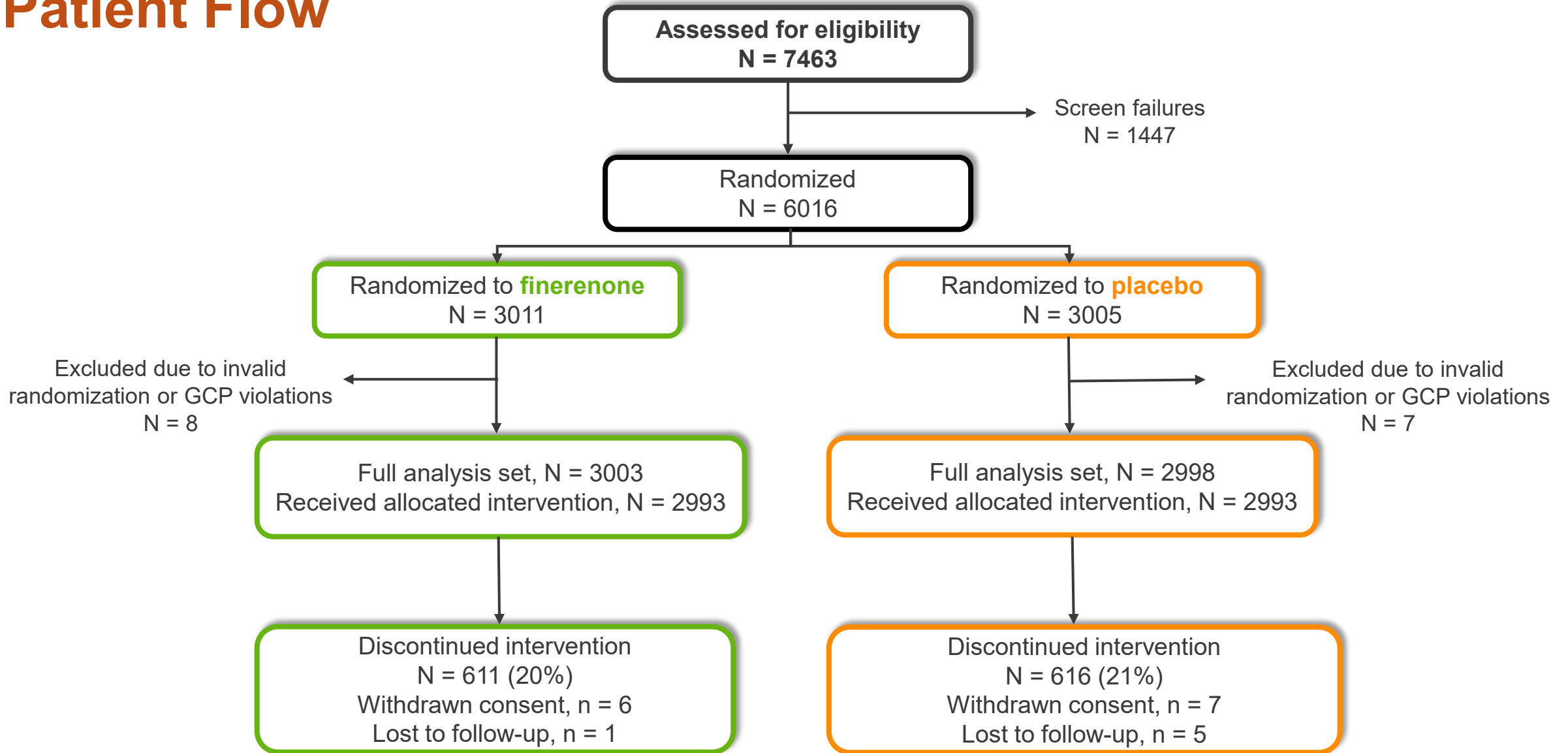


Country	Enrollment (# of Patients)
China	428
USA	355
Spain	353
Ukraine	327
Russian Federation	300
Japan	286
Bulgaria	275
Hungary	267
Slovakia	262
Poland	259
Italy	227
Greece	217
Argentina	211
Czechia	206
Romania	193
Brazil	185
Israel	181
Colombia	167
Turkey	159
Canada	116
Lithuania	100
United Kingdom	99
Portugal	88
Denmark	79
Mexico	78
Republic of Korea	74
Austria	73
Taiwan	69
Latvia	65
Netherlands	64
Malaysia	57
Hong Kong	41
New Zealand	40
Australia	32
India	28
Germany	20
Finland	20



Powered by Bing
© Australian Bureau of Statistics, GeoNames, Microsoft, Navinfo, OpenStreetMap, TomTom, Wikipedia








Patient Flow



GCP, good clinical practice

Baseline Characteristics

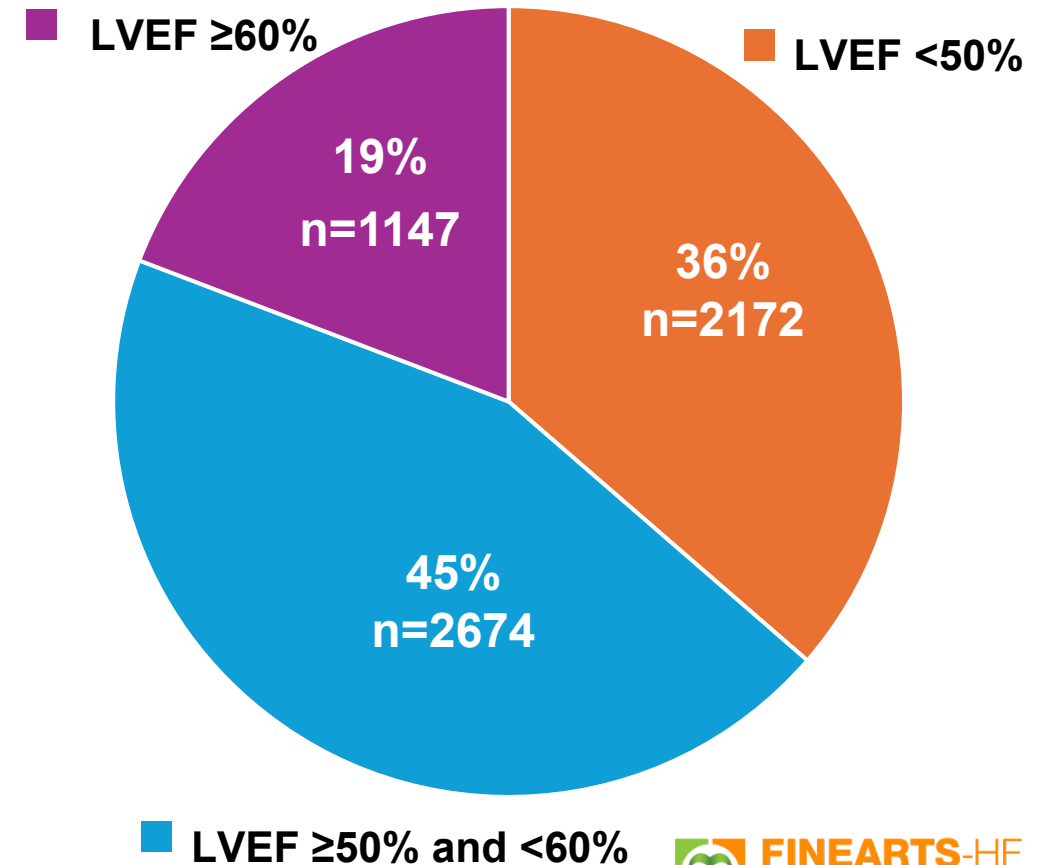
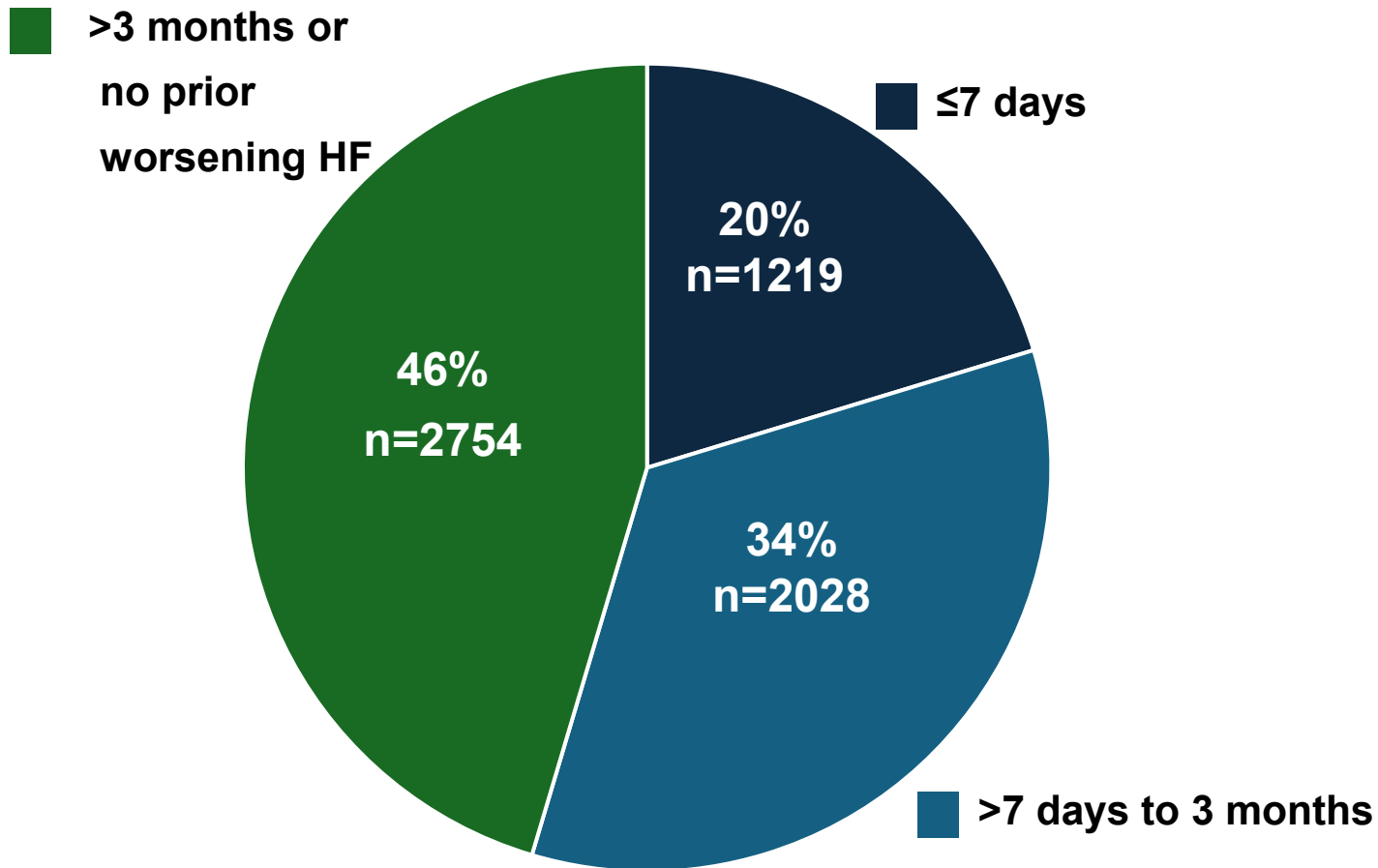
Well-balanced between treatment groups

		Finerenone N = 3003	Placebo N = 2998			Finerenone N = 3003	Placebo N = 2998
	Age	72±10	72±10		NT-proBNP (ng/L) (median)	1052	1028
	Female Sex	45%	46%		eGFR (mL/min/1.73m ²)	[467,1937]	[433,1963]
	<u>Race</u>			eGFR < 60	62±19	62±20	
	Asian	17%	17%	UACR (mg/g)	48%	48%	
	Black	2%	1%		18 [7,67]	19 [7,66]	
	Other	3%	3%		Prior HF Hospitalization	60%	61%
	White	79%	79%		History of LVEF ≤40%	5%	4%
<u>Region</u>			Type II Diabetes		41%	41%	
Asia	16%	16%	Atrial Fibrillation on ECG	38%	38%		
Eastern Europe	44%	44%	History of Hypertension	88%	90%		
Latin America	11%	11%	History of Myocardial Infarction	26%	25%		
North America	8%	8%		Loop Diuretic	87%	87%	
Western Europe, Oceania and Others	21%	21%		Beta-blocker	85%	85%	
<u>NYHA class</u>				ACE Inhibitor	36%	36%	
II	69%	69%		ARB	35%	35%	
III	30%	30%	ARNI	9%	9%		
IV	1%	1%	Calcium Channel Blockers	32%	34%		
	KCCQ-TSS	68±24	67±24		SGLT2 Inhibitor	13%	14%
	LVEF (%)	53±8	53±8				
	Systolic Blood Pressure (mmHg)	130±15	129±15				

Randomization timing relative to the most recent worsening HF event and LVEF status on randomization

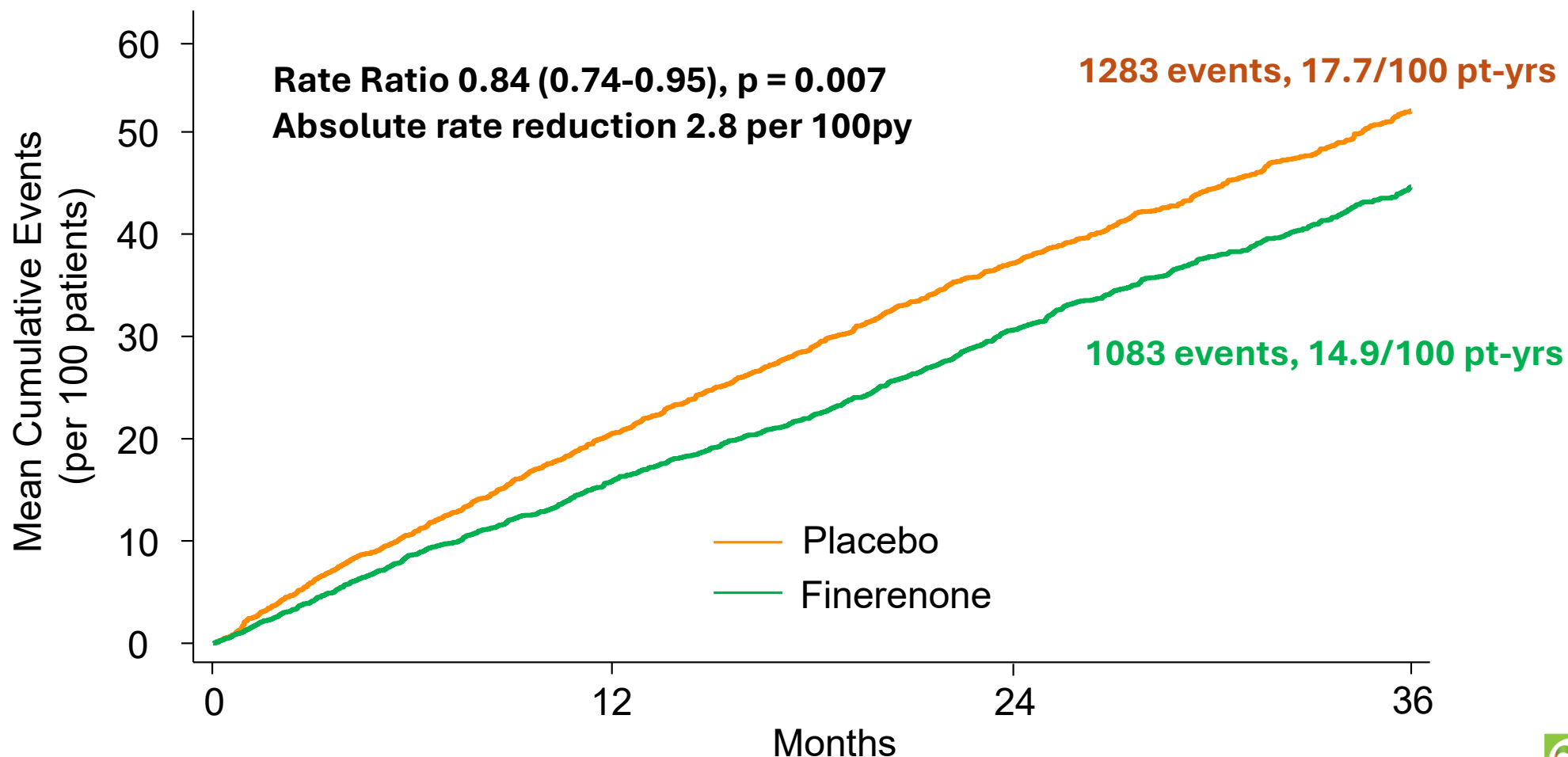
20% of participants were randomized during or within 7 days of a worsening HF event

Mean LVEF status on randomization was 53% across both treatment arms



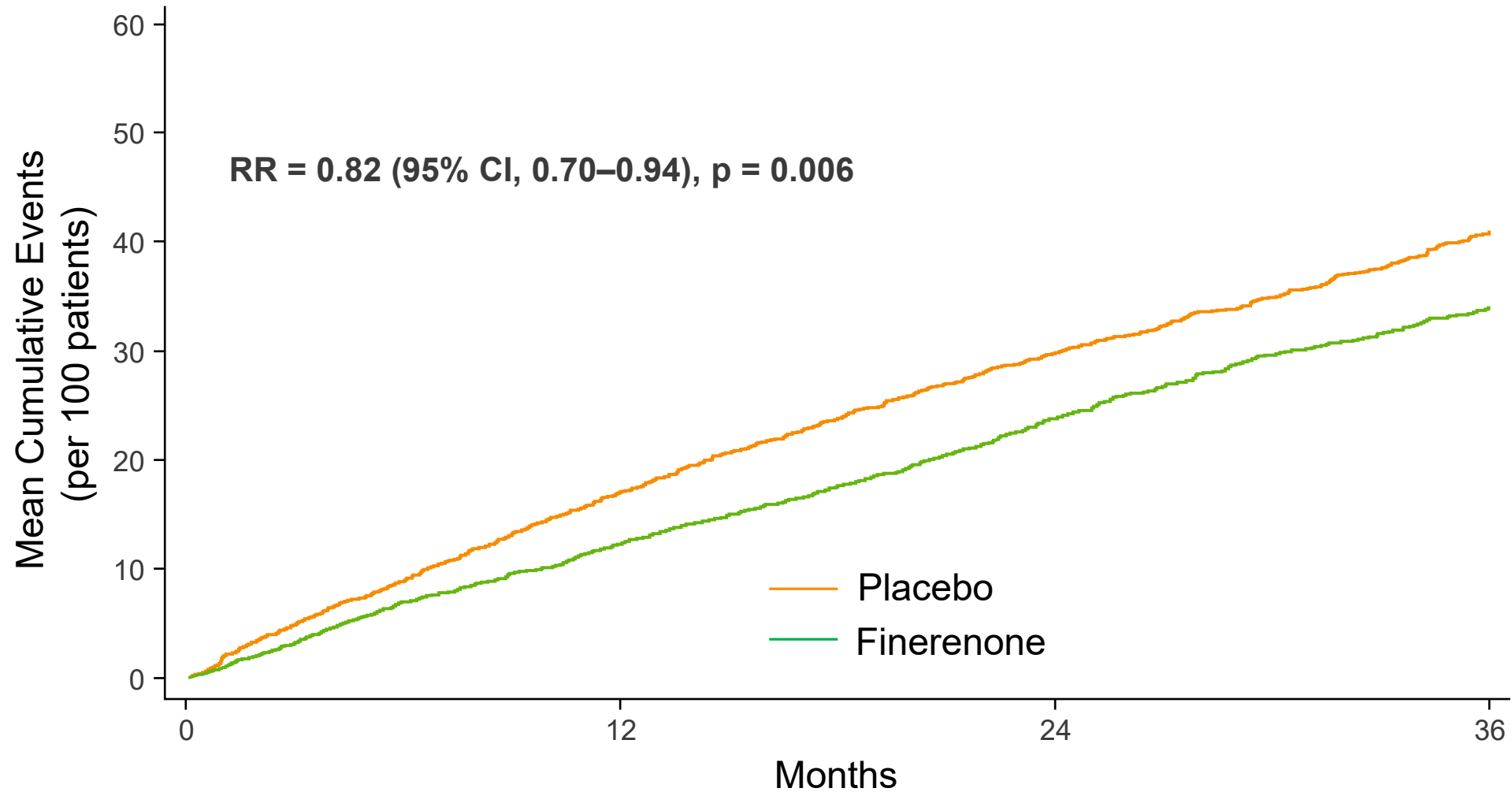
Primary Endpoint: CV Death and Total HF Events

Finerenone reduced cardiovascular death and total worsening heart failure events over median follow-up of 32 months

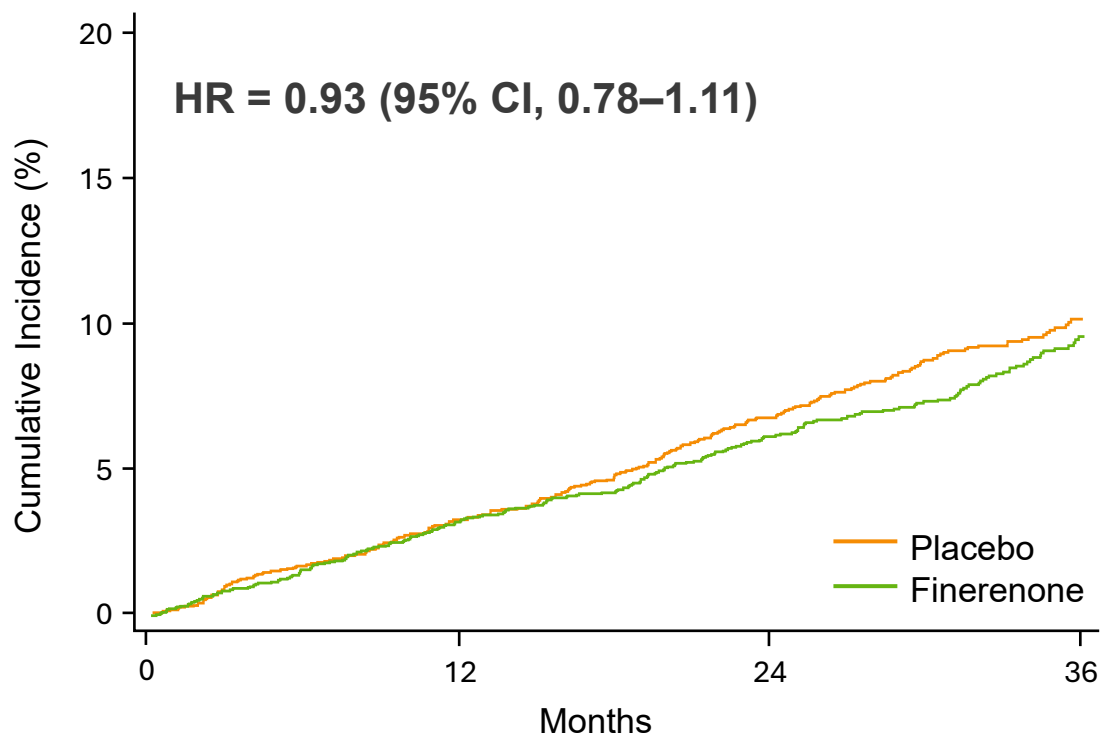


The event rates have been revised to accurately reflect the data provided in the FINEARTS-HF NEJM publication.

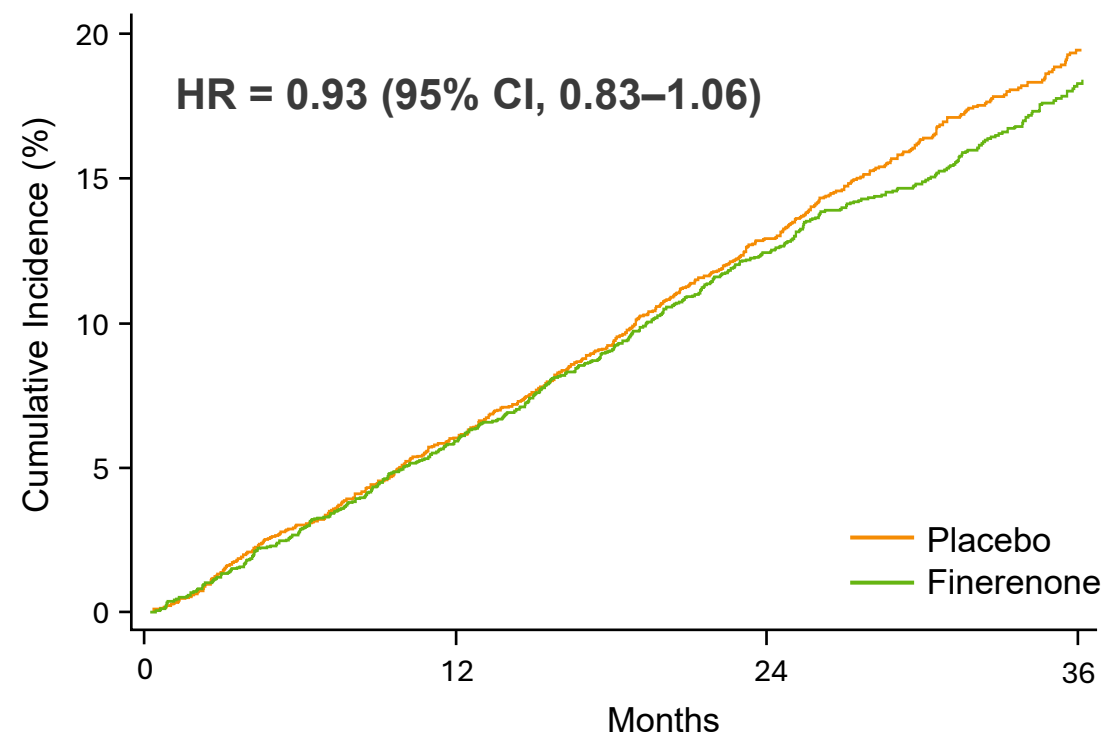
Secondary Endpoint: Total HF Events



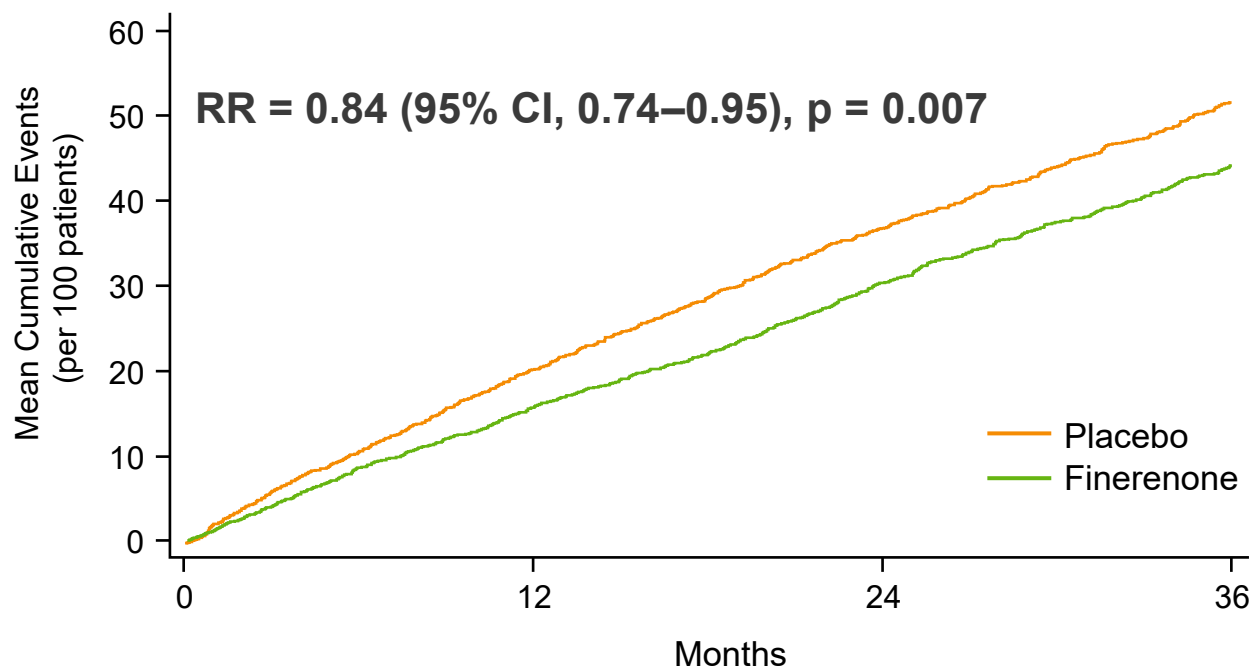
Cardiovascular Death



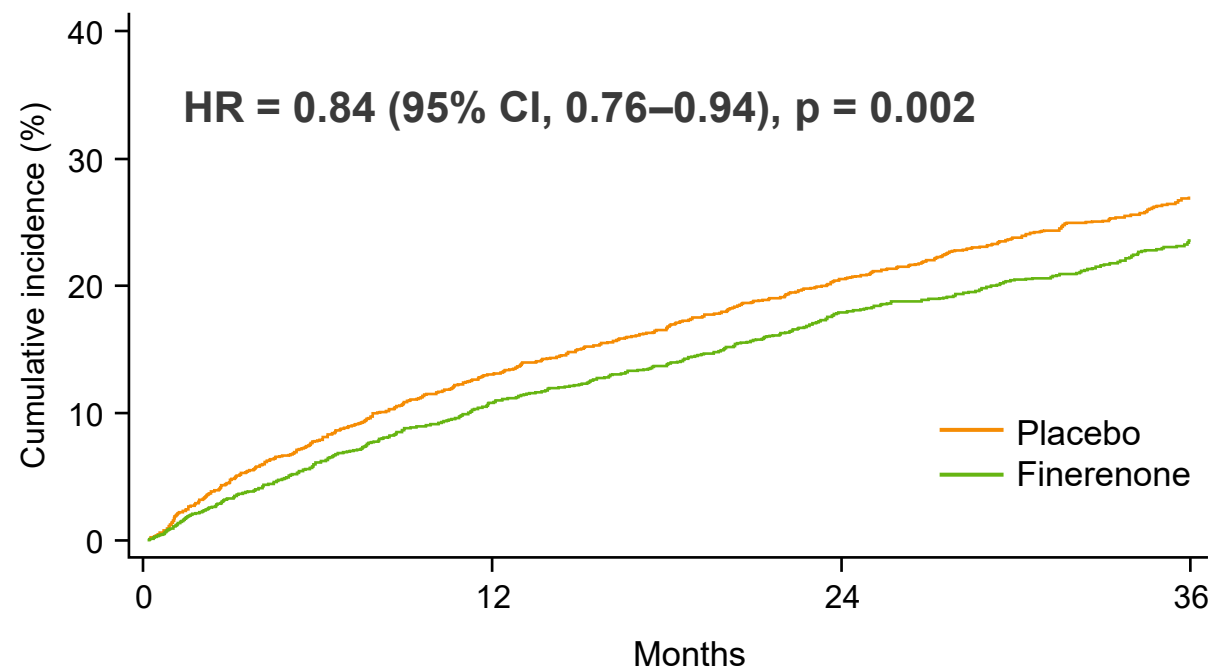
All-Cause Death



CV Death and Total HF Events

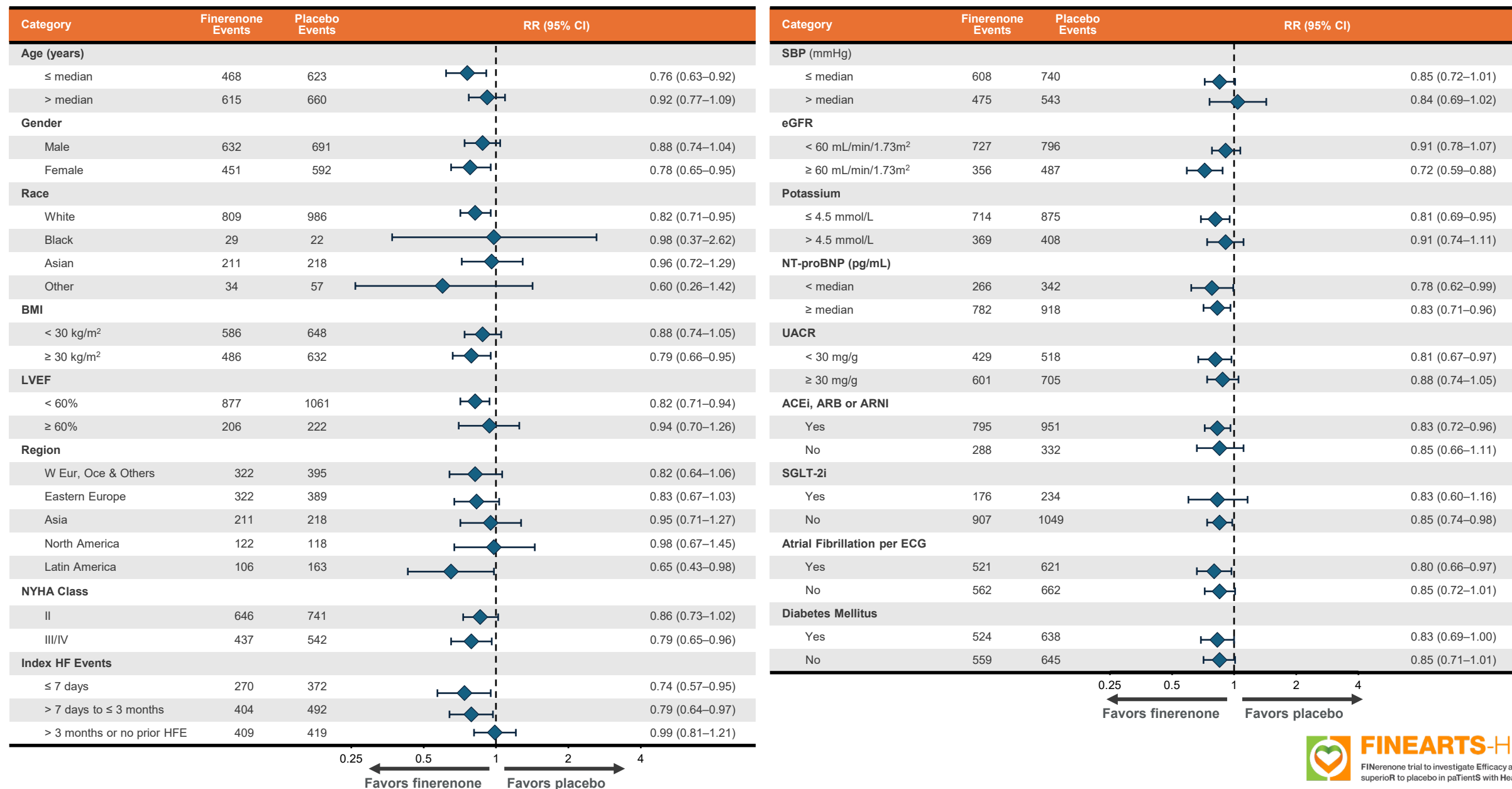


CV Death or First HF Event



Prespecified Subgroups for Primary Outcome

Consistent treatment effects across all pre-specified subgroups, including ejection fraction and SGLT2-inhibitor use



Change in KCCQ-TSS

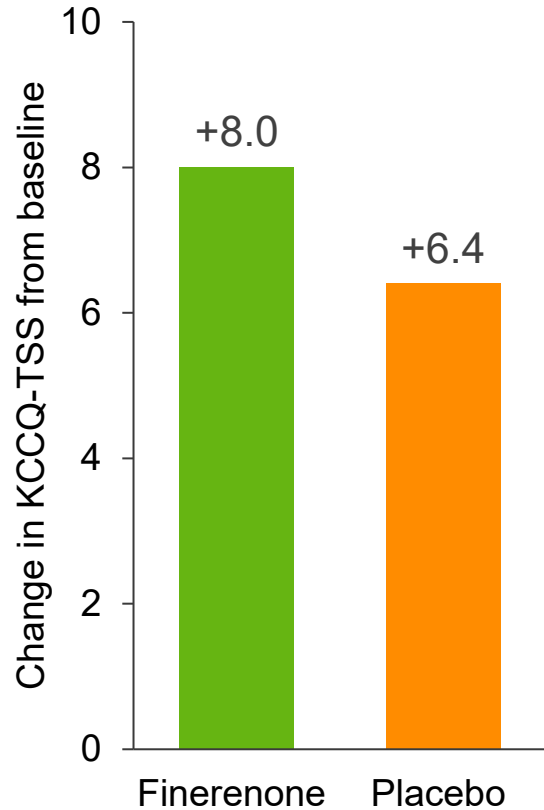
6, 9, 12 Months

Improvement in Symptom Burden

Between-arm difference:

+1.6 (0.8–2.3)

P<0.001



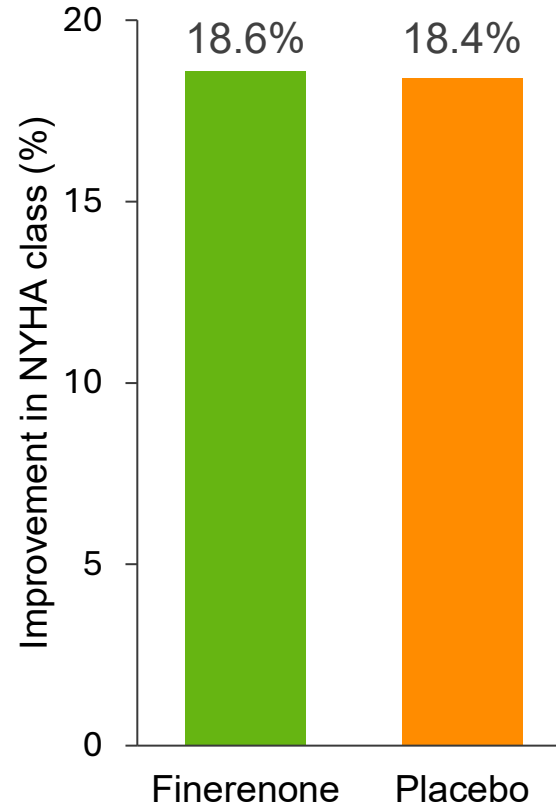
Improvement in NYHA Class

At 12 Months

No improvement in NYHA Class

OR 1.01

(95% CI, 0.88–1.15)



Renal Composite Outcome

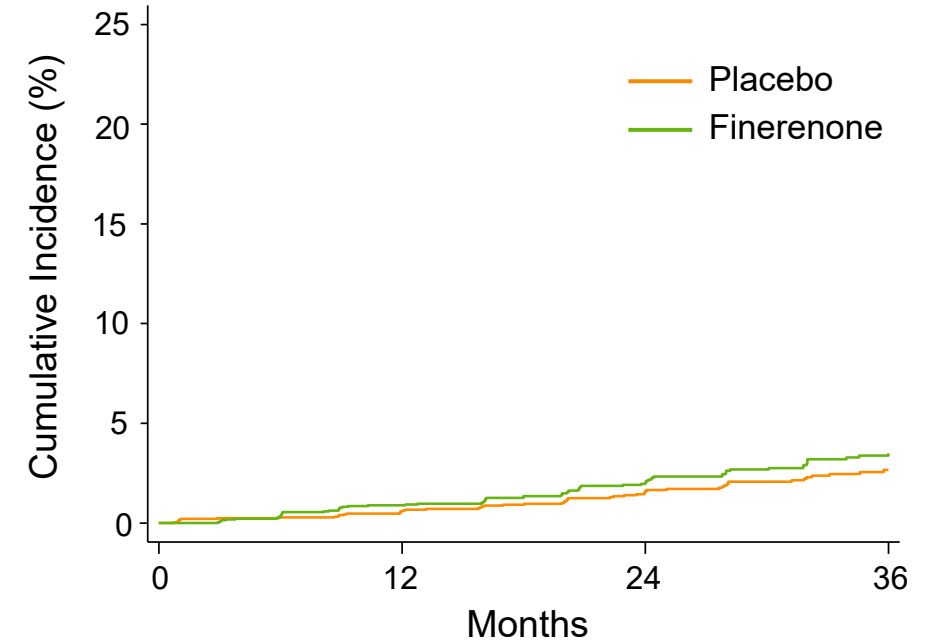
Small number of Events; No significant difference

No. of events

Finerenone 75 (2.5%)

Placebo 55 (1.8%)

HR 1.33 (95% CI, 0.94-1.89)



Safety

Treatment Emergent Safety Outcome	Finerenone (N=2993)	Placebo (N=2993)
Any Serious Adverse Event (SAE)	38.7%	40.5%
Serum creatinine \geq 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 hyperkalemia	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%

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, reduced total heart failure events, and improved overall health status
- These findings were consistent across prespecified subgroups, including across LVEF and in those on SGLT2 inhibitors
- Hyperkalemia was more common, and hypokalemia less common, in those receiving finerenone
- These data support the use of finerenone in patients with heart failure with mildly reduced or preserved ejection fraction

Steering Committee

Scott D. Solomon, MD & John J.V. McMurray, MD, Co-Chairs

Carolyn S.P. Lam, MD, Bertram Pitt, MD, Michele Senni, MD, Sanjiv Shah, MD,
Adriaan Voors, MD, Faiez Zannad, MD

Sponsor Leadership

Bayer

Prabhakar Viswanathan, MD, Ilse Van Gameren,
Flaviana Amarante, MD, James Lay-Flurrie, MSc
Catherine Salt, Michelle King, Maria Borentain, MD

Clinical Events Committee

Akshay Desai, MD, Pardeep Jhund, MD (Chairs)

Data Safety Monitoring Committee

Aldo Maggioni, MD, Murray Epstein, MD (Chairs)

Independent Statistical Team

Brian Claggett, PhD, Muthiah Vaduganathan, MD, Pardeep Jhund,
MD, Alasdair Henderson, PhD

National Lead Investigators

Argentina	Felipe Martinez
Australia	John Atherton
Austria	Dirk von Lewinski
Brazil	Jose Francisco Kerr Saraiva
Bulgaria	Tzvetana Katova
Canada	Shelley Zieroth
Canada	Jay Udell
Canada	Subodh Verma
China	Ma chang-sheng
Colombia	Clara Inés Saldarriaga
Czech Rep	Vojtěch Melenovský
Denmark	Morten Schou
Finland	Heikki Ukkonen
Germany	Johann Bauersachs
Greece	Gerasimos Filippatos
Hungary	Bela Merkely
Hong Kong	Alex Lee
India	Vijay Chopra
Israel	Sorel Goland
Italy	Savina Nodari

Japan	Naoki Sato
Latvia	Gustavs Latkovskis
Malaysia	Imran Zainal Abidin
Mexico	Marco Alcocer-Gamba
Mexico	Guillermo Llamas Esperón
Netherlands	Gerard Linssen
New Zealand	Richard Troughton
Poland	Grzegorz Gajos
Portugal	Cândida Fonseca
Romania	Ovidiu Chioncel
Russia	Vyacheslav Mareev
Slovakia	Eva Goncalvesova
South-Korea	Seokmin Kang
Spain	Josep Comin Colet
Taiwan	Chern-En Chiang
Turkey	Mehmet Birhan Yilmaz
UK	Mark Petrie
Ukraine	Leonid Voronkov
USA	Orly Vardeny
USA	Kavita Sharma
USA	Mikhail Kosiborod

We thank all the FINEARTS-HF Investigators and participants!



ORIGINAL ARTICLE

Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

S.D. Solomon, J.J.V. McMurray, M. Vaduganathan, B. Claggett, P.S. Jhund, A.S. Desai, A.D. Henderson, C.S.P. Lam, B. Pitt, M. Senni, S.J. Shah, A.A. Voors, F. Zannad, I.Z. Abidin, M.A. Alcocer-Gamba, J.J. Atherton, J. Bauersachs, M. Chang-Sheng, C.-E. Chiang, O. Chioncel, V. Chopra, J. Comin-Colet, G. Filippatos, C. Fonseca, G. Gajos, S. Goland, E. Goncalvesova, S. Kang, T. Katova, M.N. Kosiborod, G. Latkovskis, A.P.-W. Lee, G.C.M. Linssen, G. Llamas-Espesón, V. Mareev, F.A. Martinez, V. Melenovský, B. Merkely, S. Nodari, M.C. Petrie, C.I. Saldarriaga, J.F.K. Saraiva, N. Sato, M. Schou, K. Sharma, R. Troughton, J.A. Udell, H. Ukkonen, O. Vardeny, S. Verma, D. von Lewinski, L. Voronkov, M.B. Yilmaz, S. Zieroth, J. Lay-Flurrie, I. van Gameren, F. Amarante, P. Kolkhof, and P. Viswanathan, for the FINEARTS-HF Committees and Investigators*

