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

Design and Baseline Characteristics

Scott D. Solomon, MD, on behalf of the FINEARTS-HF Steering Committee

Brigham and Women's Hospital

Harvard Medical School

Boston, MA, USA

FINEARTS-HF

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

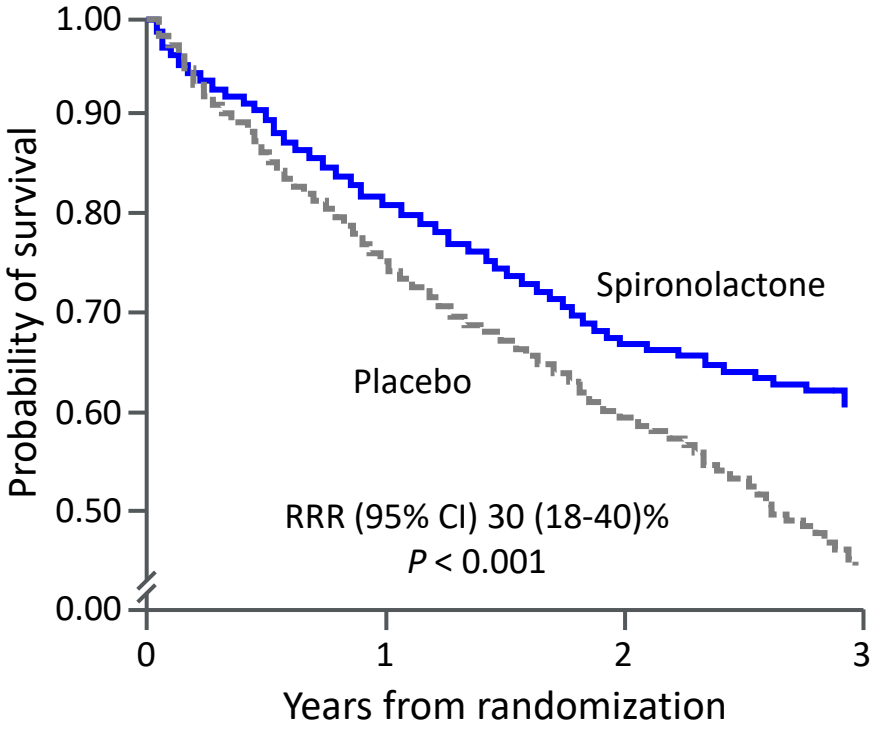
DISCLOSURES

- Dr. Solomon's has received research grants (to his institution) from the National Heart Lung and Blood Institute, Actelion, Alnylam, AstraZeneca, Bayer, BMS, Cytokinetics, Eidos/Bridgebio, GSK, Ionis, Lilly, Mesoblast, Novartis, NovoNordisk, Respicardia, Sanofi Pasteur, Theracos, US2.AI and has consulted for Abbott, Action, Akros, Alnylam, Amgen, Arena, AstraZeneca, Bayer, Boeringer-Ingelheim, BMS, Cardior, Cardurion, Corvia, Cytokinetics, Daiichi-Sankyo, GSK, Lilly, Merck, Myokardia, Novartis, Roche, Theracos, Quantum Genomics, Cardurion, Janssen, Cardiac Dimensions, Tenaya, Sanofi-Pasteur, Dinaqor, Tremeau, CellProThera, Moderna, American Regent, Sarepta, Lexicon, Anacardio, Akros, Valo
- FINEARTS-HF is sponsored by Bayer

Steroidal MRAs: a pillar of guideline-directed medical therapy for patients with HF with reduced ejection fraction

RALES (1999)

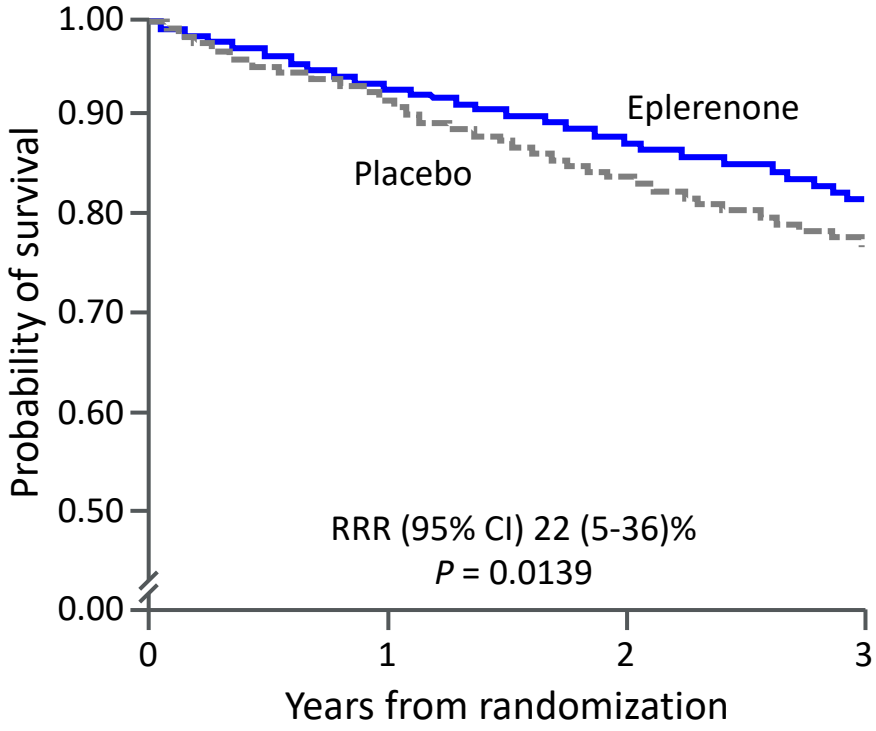
1663 NYHA class III/IV patients
95% ACE-I/10% β-blocker



Pitt B, et al. *N Engl J Med.* 1999;341:709-717.

EMPHASIS-HF (2011)

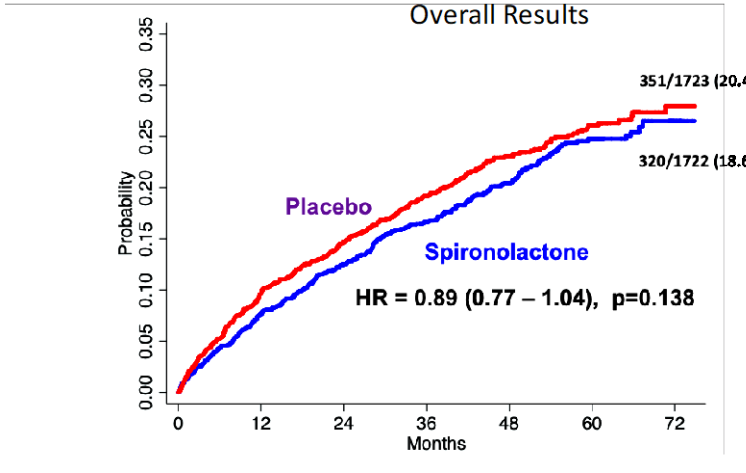
2737 NYHA class II patients
93% ACE-I or ARB/87% β-blocker



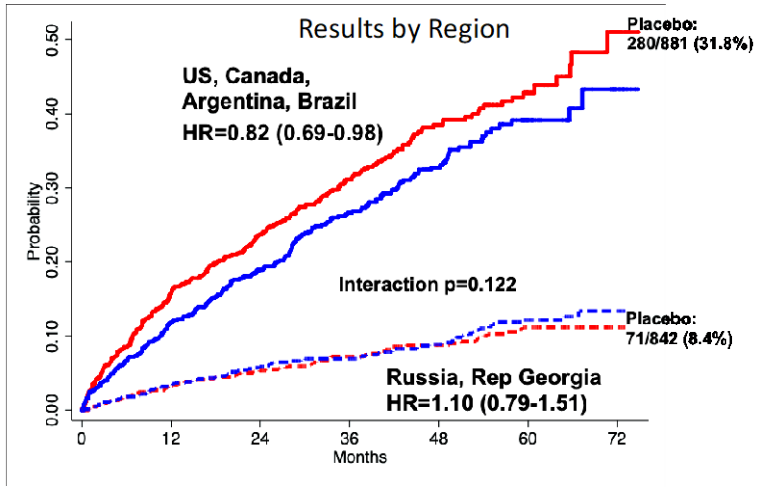
Zannad F, et al. *N Engl J Med*. 2011;364:11-21.

TOPCAT: A tale of two populations
Missed Primary Endpoint in HFpEF but Suggestive of Benefit in Some Patients
Concern in patients with worse renal function

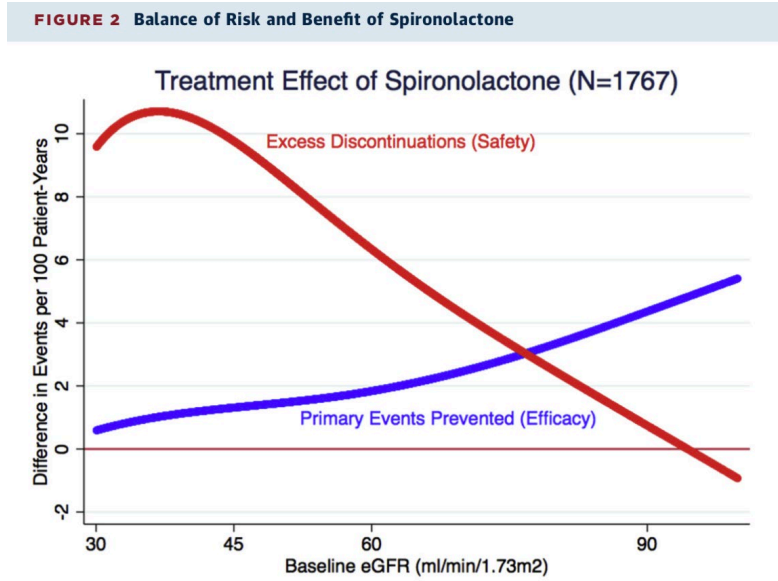
CV Death, HF Hospitalization or Cardiac Arrest



Pitt et al. NEJM 2014;370(15):1383-92

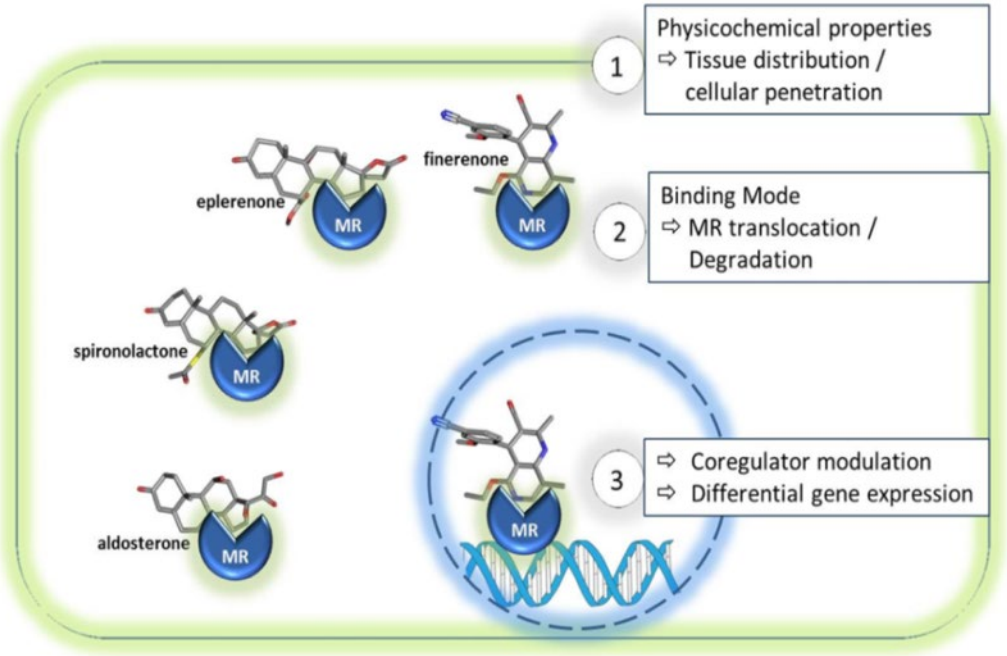


Pfeffer MA et al. Circulation. 2015 Jan 6;131(1):34-42



Beldhuis I et al. JACC 2019

Finerenone is a potent, highly selective non-steroidal MRA with Equivalent Heart: Kidney Tissue Distribution and Potential Safety Advantages over steroidal MRAs



Kolkhof P, Nowack C, Eitner F. *Curr Opin Nephrol Hypertens.* 2015;24:417-424.

	Spironolactone	Eplerenone	Finerenone
MRA Class	Steroidal	Steroidal	Non-steroidal
Potency	High	Low	High
Selectivity	Low	Medium	High
Metabolites	Multiple, active	No active	No active
Tissue distribution	Kidney>>heart (>6-fold)	Kidney>heart (~3-fold)	Equivalent (1:1)

- More selective for MR receptor than spironolactone or eplerenone
- Highly potent
- More balanced Heart/Kidney Distribution than steroidal MRAs

Kolkhof P et al. *Handb Exp Pharmacol.* 2017;243:271-305

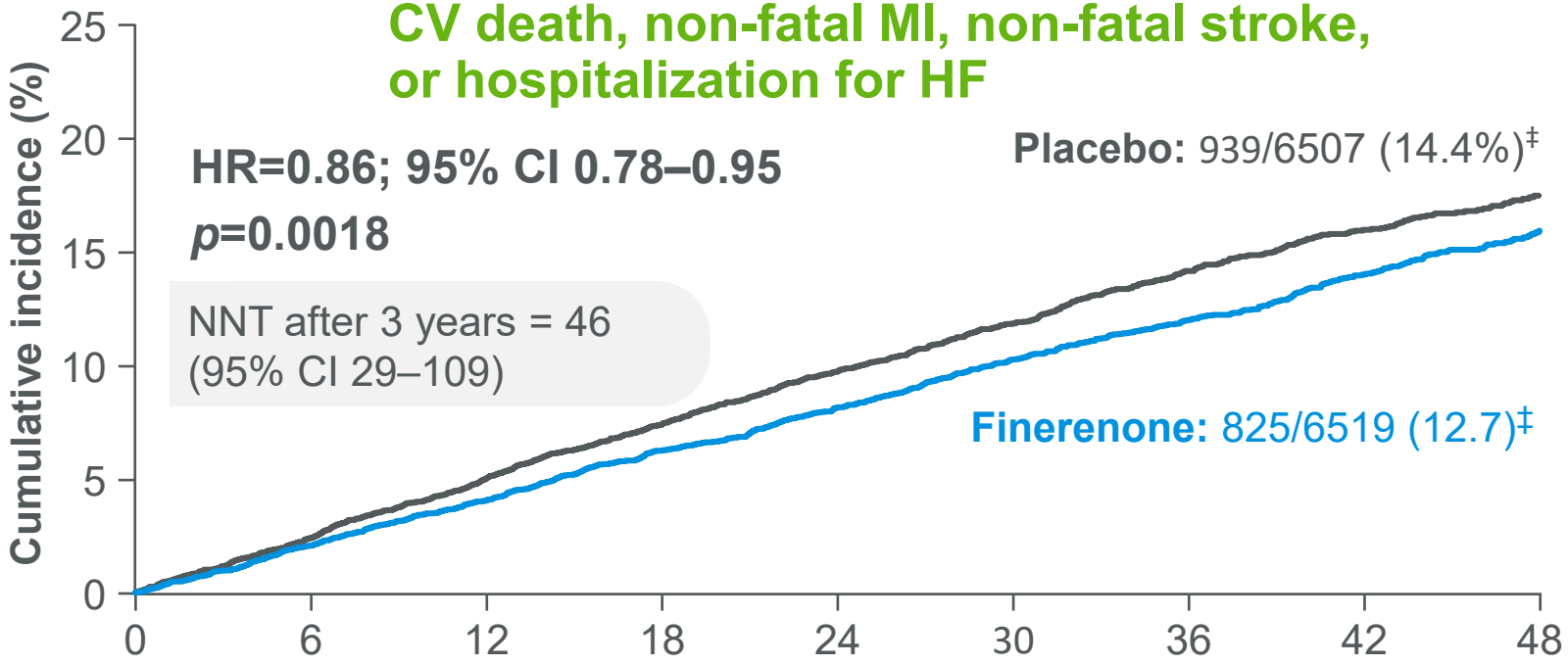
Finerenone effective in reducing cardiovascular and renal events in type 2 diabetes and CKD

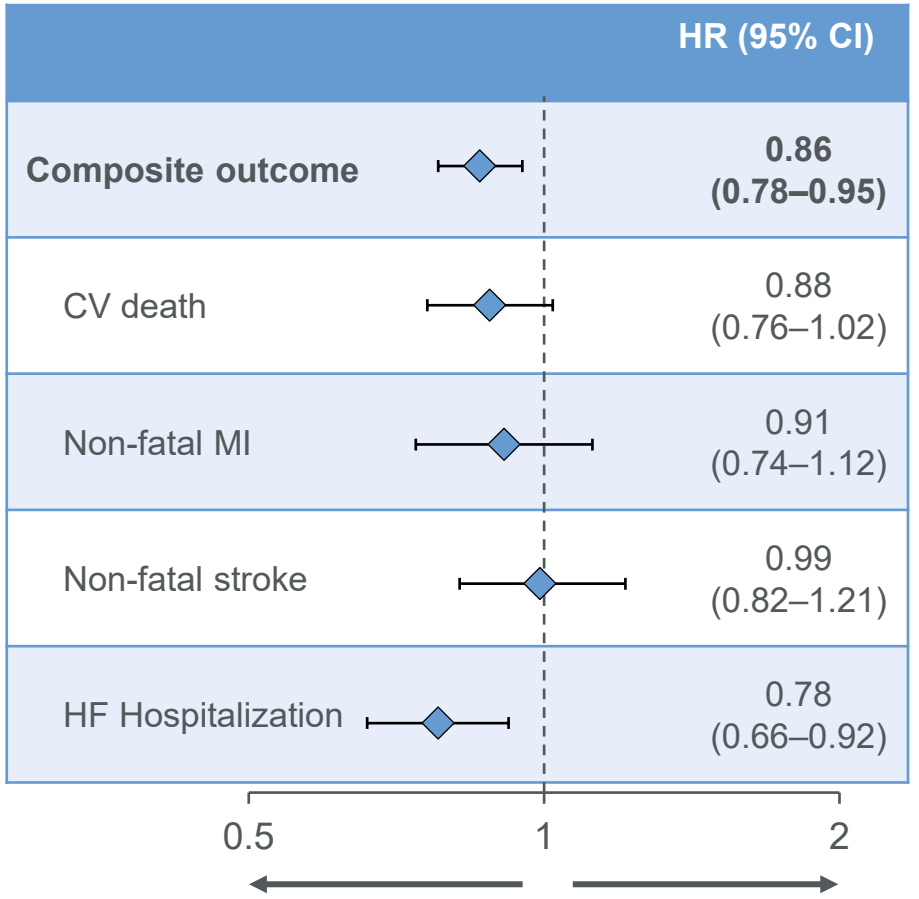
Inclusion/Exclusion

T2D+CKD
eGFR ≥ 25 mL/min/1.73m2
Serum K+ ≤ 4.8 mmol/L
Maximal tolerated dose of RAS
No HFrEF

FIDELIO-DKD and FIGARO-DKD Pooled Analysis:

Finerenone significantly ↓ risk of primary CV composite outcome, including fewer hospitalizations for HF



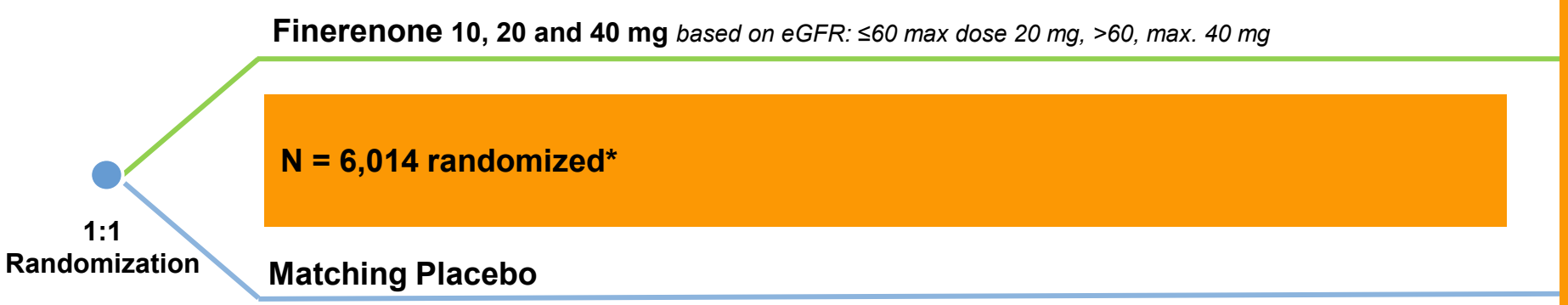


*Cumulative incidence calculated by Aalen–Johansen estimator using deaths due to other causes as competing risk; #at-risk subjects were calculated at start of time point; ‡number of patients with an event over a median of 3.0 years of follow-up

Agarwal R, et al. Eur Heart J 2022

Design, Endpoints & Eligibility Criteria

FINEARTS-HF designed to evaluate the efficacy and safety of finerenone in patients with HF and LVEF ≥40%, with or without diabetes, and across a broad range of renal function



Study Endpoints

Primary Endpoint

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

Secondary Endpoints

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

Key Inclusion Criteria

- **Symptomatic HF (NYHA class II-V) with LVEF ≥ 40%**
  - *LVEF ≥ 60% capped at 20%*
- **Hospitalized, Recently Hospitalized, or Ambulatory**
- **Elevated Natriuretic Peptide Levels (300/900 AF)**
- **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**
- **MI or PCI 30d prior to randomization**
- **Cardiogenic shock**
- **History of dilated, peripartum, chemotherapy induced, or infiltrative cardiomyopathy (e.g., amyloidosis)**
- **Alternative causes of signs or symptoms**

*validly randomized patients = 6014

FINEARTS-HF

FINEARTS-HF includes patients with LVEF ≥40% and eGFR ≥25 ml/min/1.73 m², with or without DM

Main inclusion criteria

- **Aged ≥40 years**
- **HF diagnosis with NYHA class II–IV**
- **LVEF ≥40% (**LVEF ≥ 60% capped at 20%)
- **Structrual Heart Disease**
- **eGFR ≥25** ml/min/1.73 m²
- **Serum [K⁺] ≤5.0** mmol/l

	In patients with sinus rhythm:	In patients with AF:
[K⁺]	NT-proBNP ≥300 pg/ml	NT-proBNP ≥900 pg/ml
	or	or
	BNP ≥100 pg/ml	BNP ≥300 pg/ml

Main exclusion criteria

- **eGFR <25** ml/min/1.73 m²
- **Serum [K⁺] >5.0** mmol/l
- **MI** or any event that could have **reduced the EF** within 90 days prior to randomisation
- **History of Dilated, peripartum, chemotherapy induced or infiltrative cardiomyopathy (i.e. amyloidosis)**
- **Alternative causes of signs or symptoms**
- **MRA use within 30 days of randomization**
- **SBP ≥160** mmHg

FINEARTS-HF

FINEARTS Primary and Secondary Outcomes

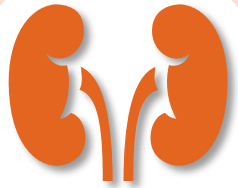
Primary outcome

Number and Timing of **CV deaths** and Total **HF events**

HF events are:

- First and recurrent events
- HHF or urgent care visit for HF

2375 First and Recurrent Events Targeted



Secondary outcomes

Total HF events
(first and recurrent)

Improvement in **NYHA class** from baseline to Month 12

Change in **KCCQ-TSS** (from baseline to months 6, 9 and 12)

Time to first occurrence of the **composite kidney endpoint:**

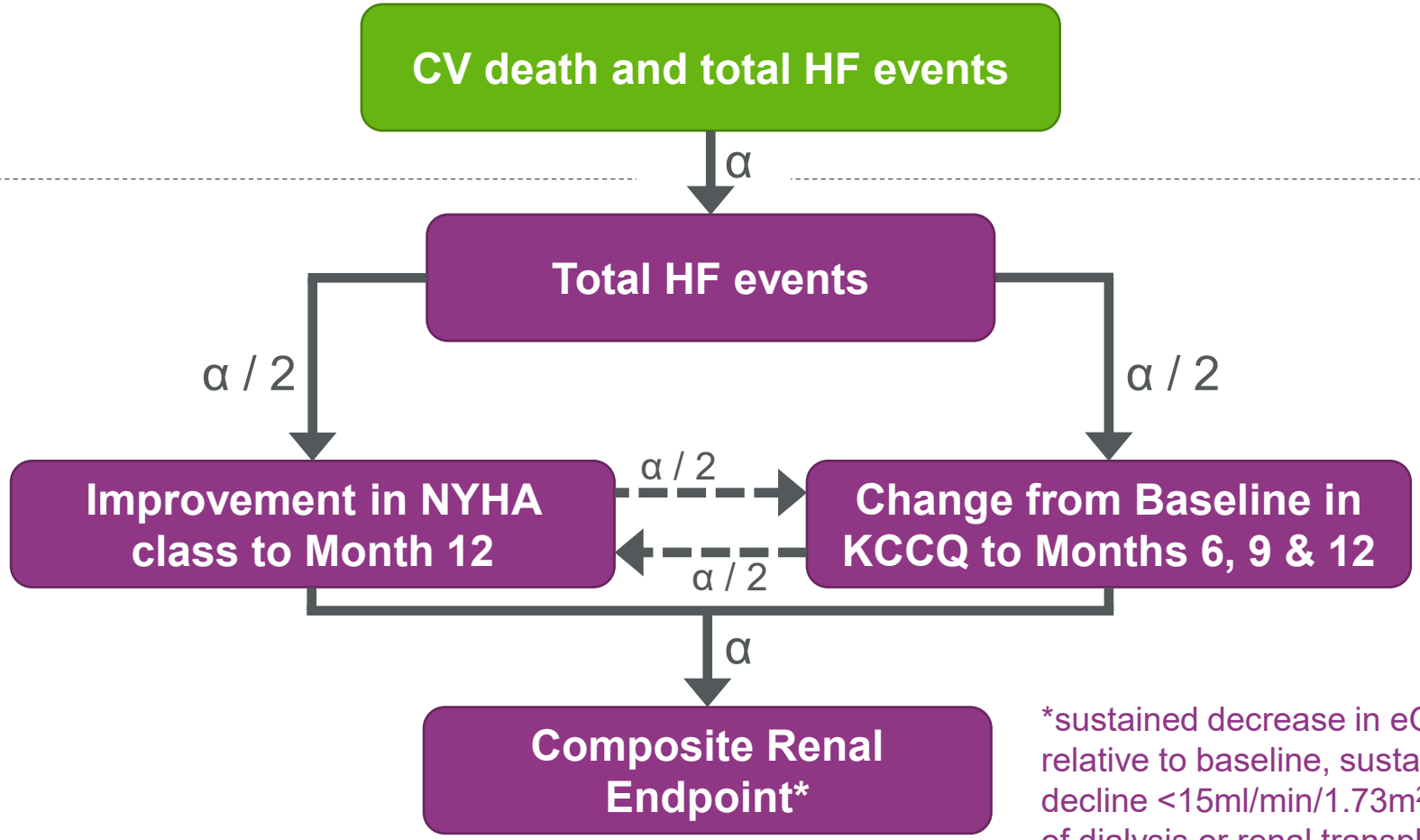
- Sustained decrease in eGFR ≥50% relative to baseline for ≥4 weeks
- Sustained eGFR decline <15 ml/min/1.73 m^2
- Initiation of dialysis or kidney transplantation

Time to **death from any cause**

FINEARTS-HF

FINEARTS-HF Primary and Secondary Outcomes

Primary and Secondary (including testing strategy)



Primary endpoint

Secondary endpoints

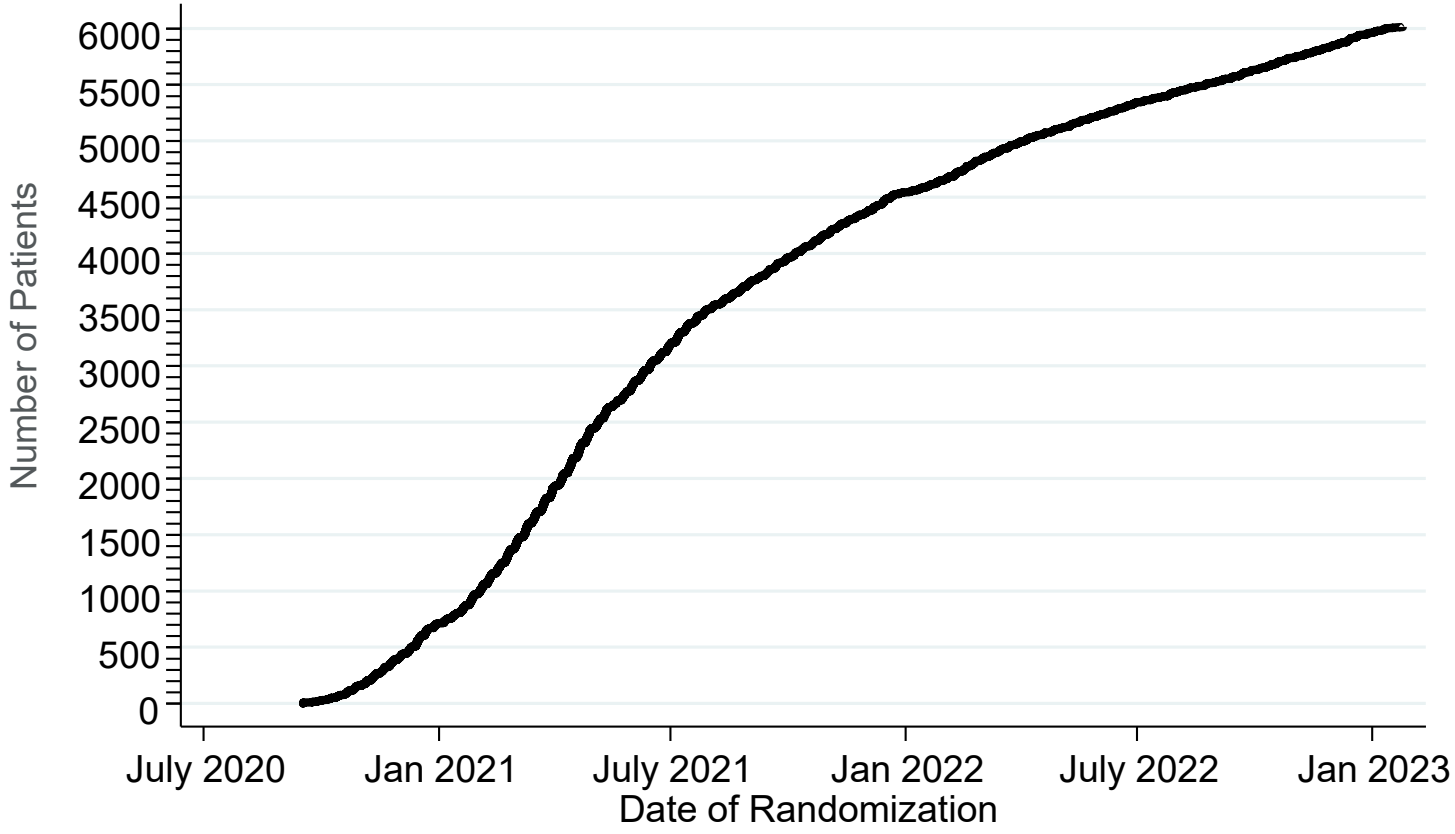
All-cause mortality#

#ACM is tested at α=0.05 outside the format testing strategy

*sustained decrease in eGFR ≥50% relative to baseline, sustained eGFR decline <15ml/min/1.73m^2, initiation of dialysis or renal transplantation

FINEARTS-HF

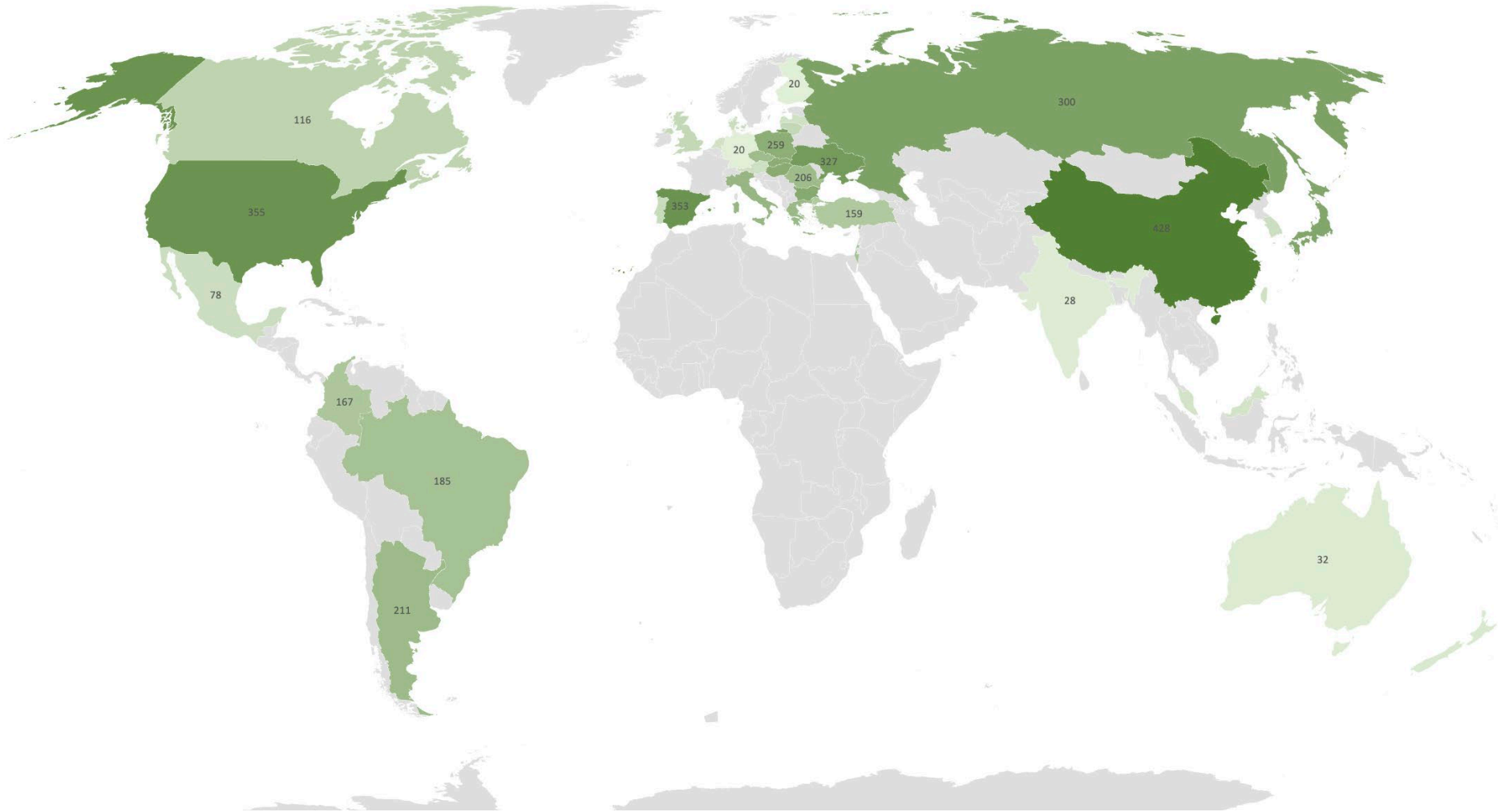
Recruitment: 6014* Patients over 28 Months



* 2 patients were invalidly randomized and will not be included in the final efficacy analyses

FINEARTS-HF

Global Randomization Across 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	206
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

FINEARTS-HF

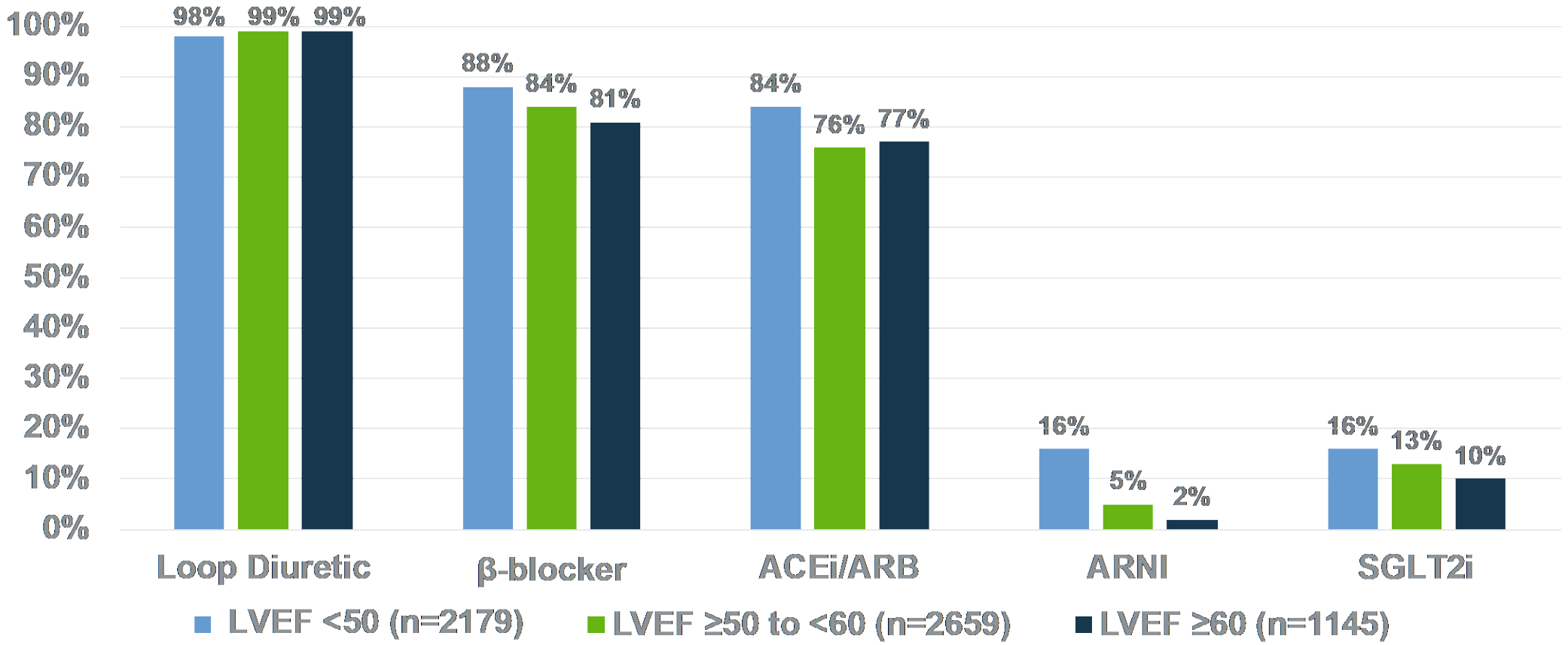
Baseline Characteristics

	All FINEARTS-HF Participants (n=6014)
Age	72±10
Female Sex	45%
BMI (kg/m2)	30±6
Race	
Asian	17%
Black	2%
Other	3%
White	79%
Asia	16%
Eastern Europe	44%
Latin America	11%
North America	8%
Western Europe, Oceania and Others	21%
NYHA class	
II	69%
III	30%
IV	0.7%
KCCQ-TSS	67±24
LVEF (%)	53±8
AF/Flutter on Enrollment	39%
Heart Rate (beats/min)	71±12
Systolic Blood Pressure (mmHg)	129±15
NT-proBNP (ng/L) (median)	1502
eGFR (mL/min/1.73m^2)	62±20
eGFR >=60	52%
Prior HF Hospitalization	60%
History of LVEF <=40%	5%
History of Diabetes	41%
History of Atrial Flutter/Fibrillation	55%
History of Hypertension	89%
History of Myocardial Infarction	26%
History of Stroke	14%
Diuretic	98%
Beta-blocker	85%
Ace Inhibitor (ACEi)	36%
Angiotensin Receptor Blocker (ARB)	44%
Angiotensin Receptor-Neprilysin Inhibitor (ARNI)	9%
Calcium Channel Blockers	33%
Sodium-glucose Cotransporter-2 Inhibitor (SGLT-2i)	14%

Baseline Characteristics by Ejection Fraction

	LVEF <50 (n=2179; 36%)	LVEF ≥50 to <60 (n=2659; 44%)	LVEF ≥60 (n=1145; 19%)	P-value
Age	70±10	73±9	74±9	<0.001
Female Sex	31%	51%	59%	<0.001
LVEF (%)	44±3	54±3	64±5	<0.001
NYHA class				0.31
II	69%	68%	71%	
III	31%	31%	28%	
IV	0.6%	0.9%	0.5%	
KCCQ-TSS	69±24	66±24	66±24	<0.001
eGFR (mL/min/1.73m^2)	65±20	61±19	60±19	<0.001
NT-proBNP (ng/L) (median)	1661	1470	1305	<0.001
History of Atrial Flutter/Fibrillation	50%	59%	55%	<0.001
History of Diabetes	40%	41%	41%	0.72
Prior HF Hospitalization	67%	59%	51%	<0.001
History of LVEF <=40%	9%	3%	1%	<0.001

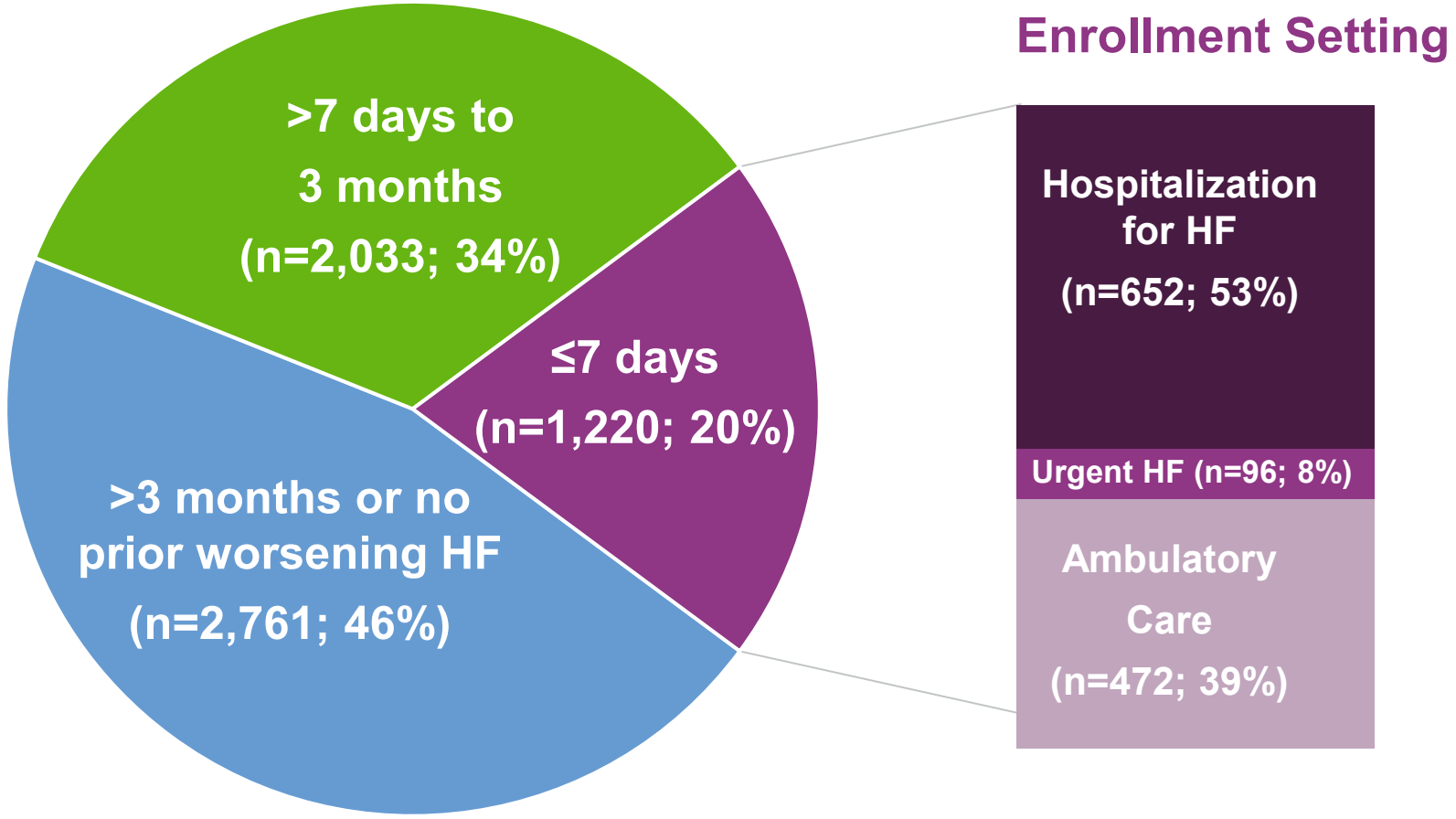
FINEARTS-HF Background Medical Therapy by Baseline LVEF



FINEARTS-HF

Enrollment Timing Relative to Most Recent Worsening HF Event

20% of participants were enrolled within 7 days and >50% enrolled within 3 months of a worsening HF event



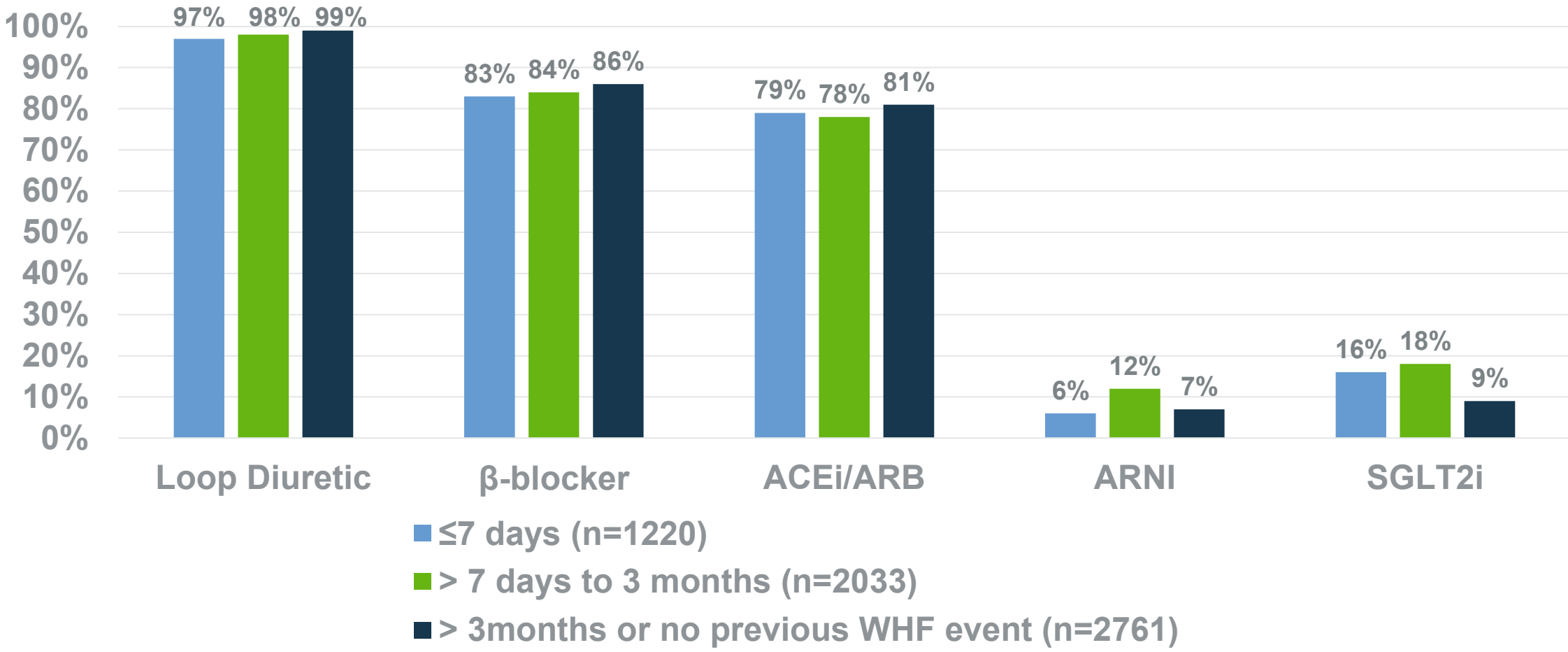
FINEARTS-HF

Baseline Characteristics in Patients Recently Hospitalized

FINEARTS-HF

	HHF <= 7 Days Before Randomization (n=1220)	HHF between > 7 days and <= 3 Months Before Randomization (n=2033)	HHF >3 Months Before Randomization or no Prior HHF (n=2761)	P-value
Age	72±10	71±10	72±9	<0.001
Female Sex	48%	46%	44%	0.11
LVEF (%)	52±8	52±7	54±8	<0.001
NYHA class				<0.001
II	51%	72%	75%	
III	47%	28%	25%	
IV	1.9%	0.6%	0.2%	
KCCQ-TSS	53±24	70±23	71±22	<0.001
eGFR (mL/min/1.73m^2)	60±20	63±20	62±19	<0.001
NT-proBNP (ng/L) (median)	1790	1691	1322	<0.001
History of Atrial Flutter/Fibrillation	61%	55%	53%	<0.001
History of Diabetes	42%	41%	40%	0.50
Prior HF Hospitalization	88%	83%	32%	<0.001

FINEARTS-HF Background Medical Therapy by Recency of Worsening HF Event



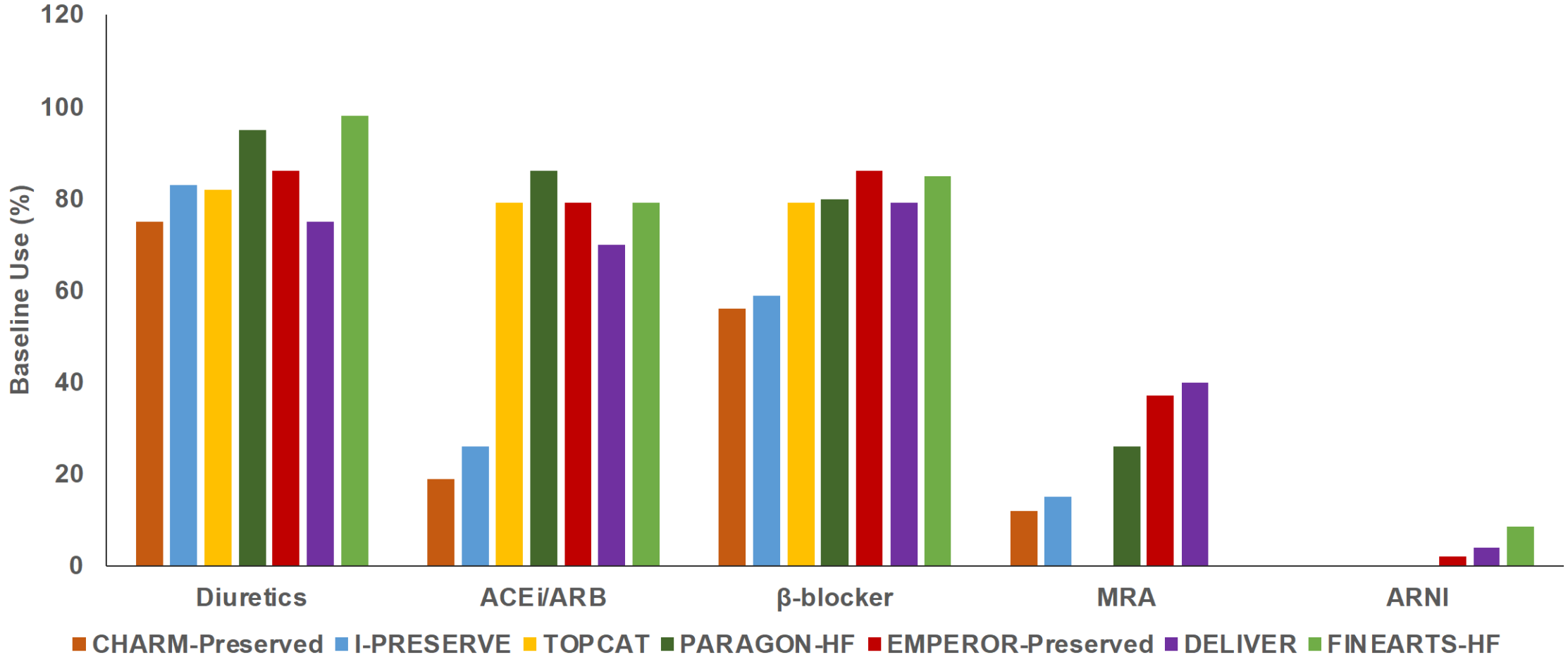
FINEARTS-HF

Baseline Characteristics - FINEARTS-HF and other HFpEF trials

	CHARM Preserved (n=3023)	EMPEROR Preserved (n=5988)	PARAGON- HF (n=4822)	TOPCAT (n=3445)	DELIVER HF (N=6263)	FINEARTS-HF (N=6014)
Age (years)	67±11	72±9	73±8	69±10	72±10	71±12
Women (%)	40	45	52	52	44	45
NYHA II (%)	61	82	72	63	75	69
NYHA III (%)	38	18	27	33	25	30
NYHA IV (%)	2	0.3	0.6	<1	0.3	0.7
LVEF (%)	54±9	54±9	58±8	57±7	54±9	53±8
Hypertension (%)	64	90	96	91	89	89
Diabetes (%)	28	49	43	32	45	41
Hx of MI (%)	44	29	23	26	26	26
Hx of AF (%)	29	52	52	35	56	55
Stroke (%)	9	10	10	8	9	14
Baseline NT-proBNP (pg/mL) – median	NA	971 (499-1740)	885 (863-908)	950 (588-1920)	1011 (623-1751)	1502
eGFR (mL/min)	NA	61±20	63±19	68±20	61±19	62±20

Date snapshot: 08 Mar 2023 Source: J-Review

Baseline Medication Use in Contemporary Trials of HFpEF



Conclusions

- FINEARTS-HF will be a broadly inclusive trial of patients with heart failure and mildly reduced or preserved ejection fraction
- FINEARTS-HF will:
  - have the highest percentage of hospitalized or recently hospitalized patients of any contemporary HFmrEF/HFpEF outcomes trial
  - be the first outcomes trial to test the efficacy of finerenone in patients without diabetes and across a broad range of renal function
  - combine data with FIDELITY (FIDELIO and FIGARO) in a pre-specified pooled patient-level analysis

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

Prabahkar Viswanathan, Ilse van Gameren, Flaviana Amarante, James Lay-Flurrie, Catherine Salt, Michelle King, Richard Nkulikiyinka, Lothar Roessig, Maria Borentain

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

Data Safety Monitoring Committee
Aldo Maggione, MD, Murray Epstein, MD (Chairs)

Independent Statistical Team
Brian Claggett,PhD, Muthiah Vaduganathan,PhD, Pardeep Jhund, PhD

FINEARTS-HF

FINerenone trial to investigate **E**fficacy and s**A**fety superio**R** to placebo in pa**T**ient**S** with **H**eart **F**ailure

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