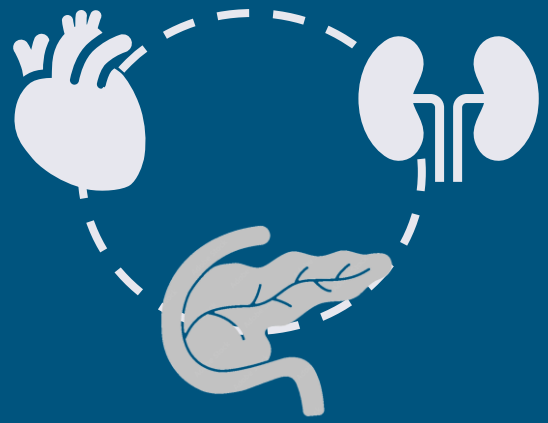
Design and Baseline Characteristics of FINE-HEART: An Integrated Pooled Analysis of Finerenone in >19,000 Participants across 3 Phase III Trials of HF, CKD & T2D



Muthiah Vaduganathan, MD MPH

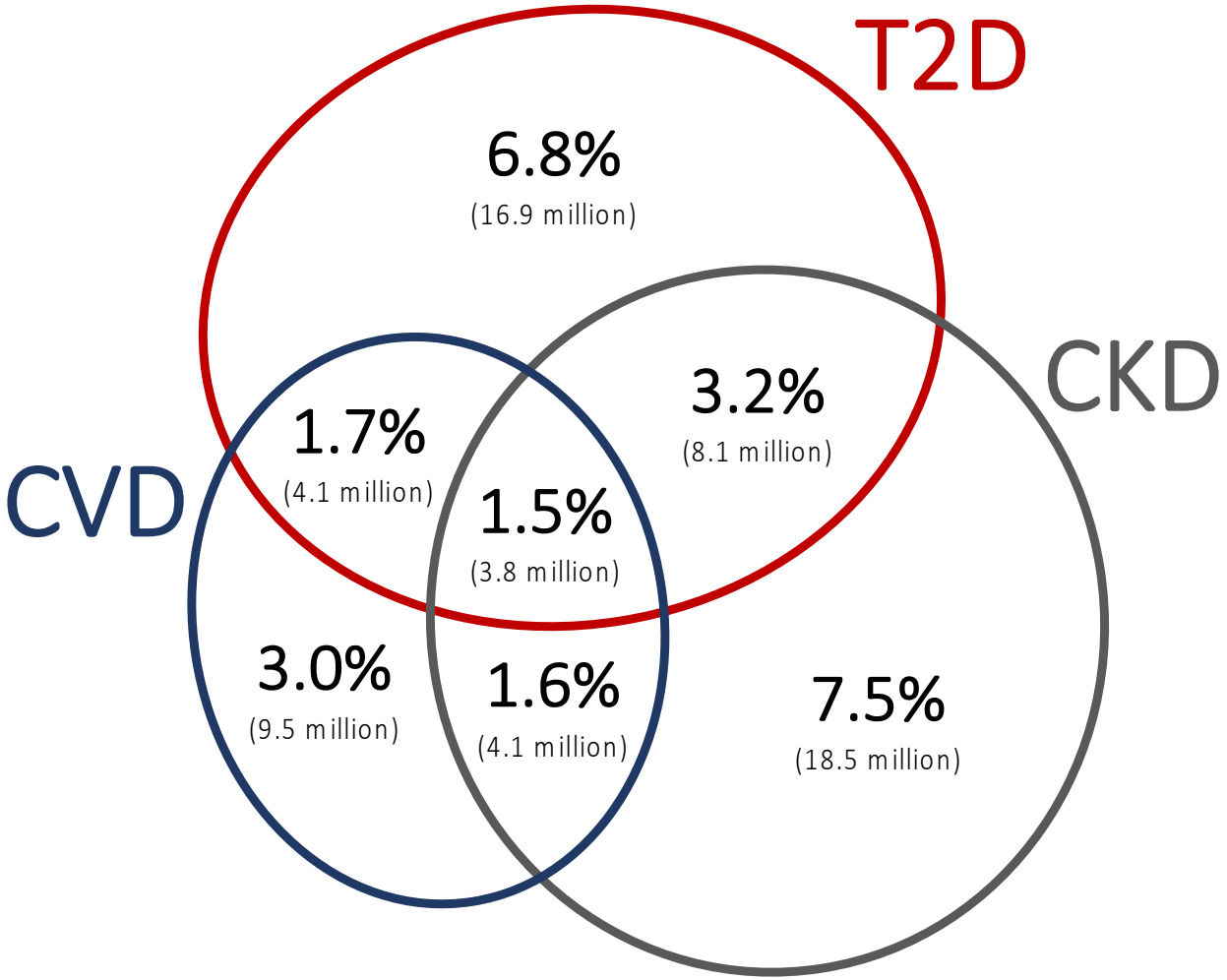
Brigham and Women's Hospital

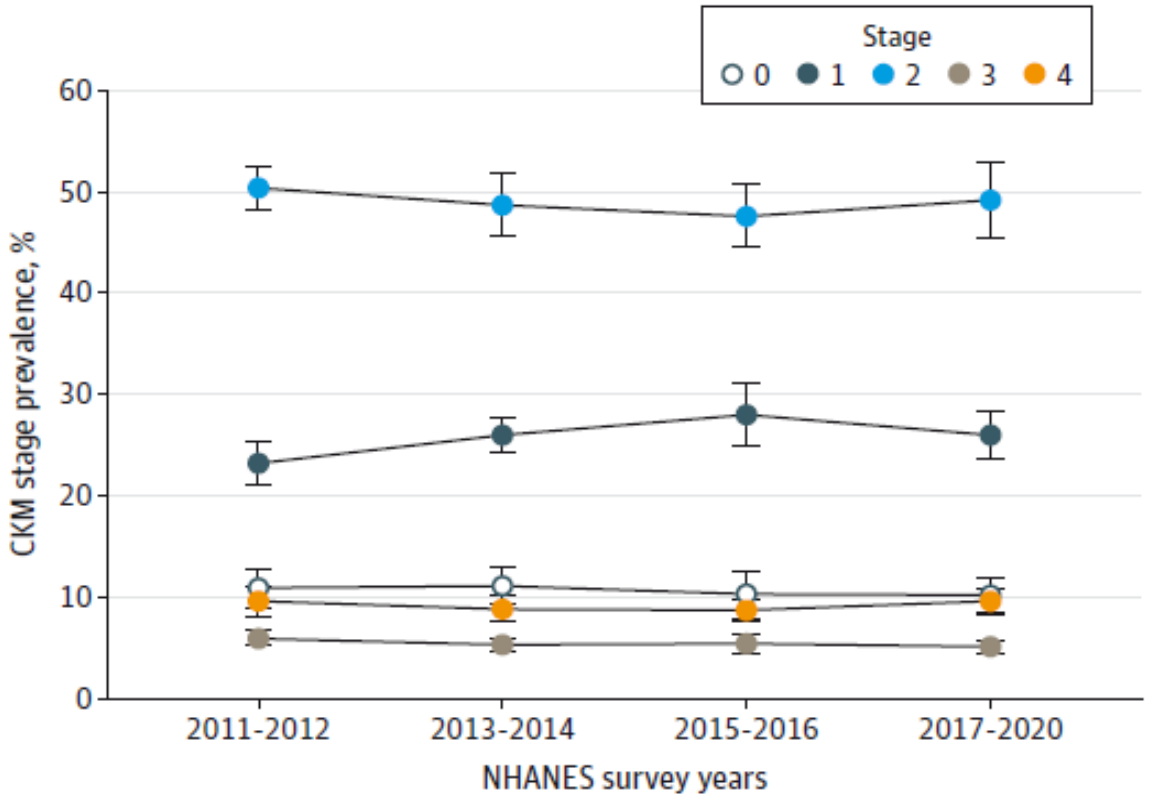
Harvard Medical School

@mvaduganathan

Disclosures: Amgen, AstraZeneca, Baxter Healthcare, Bayer AG, BMS, Boehringer Ingelheim, Chiesi, Cytokinetics, Impulse Dynamics, Lexicon Pharmaceuticals, Merck, Novartis, Novo Nordisk, Occlutech, Pharmacosmos, Relypsa, Roche Diagnostics, Sanofi, and Tricog Health

Strong Epidemiological Overlap of Cardiovascular, Metabolic, and Kidney Disorders

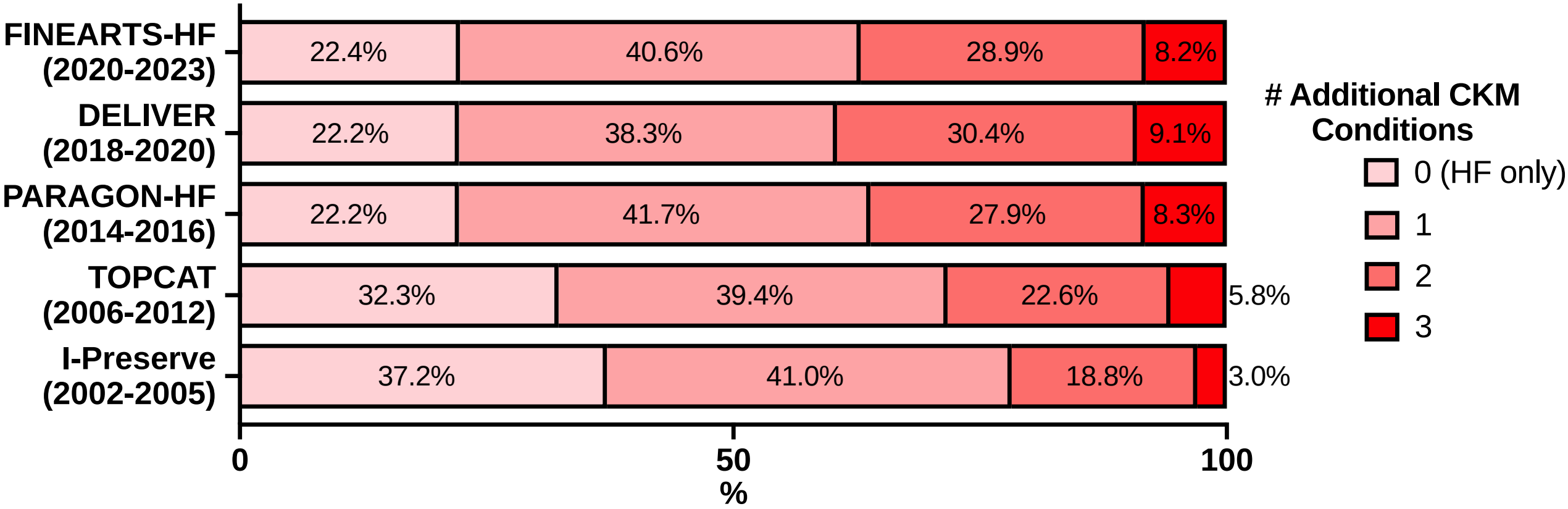




US NHANES Survey Cycles 1999-2020
Ostrominski J…Vaduganathan M. JAMA Cardiology 2023

US NHANES Survey Cycles 2011-2020
Aggarwal R…Vaduganathan M. JAMA 2024

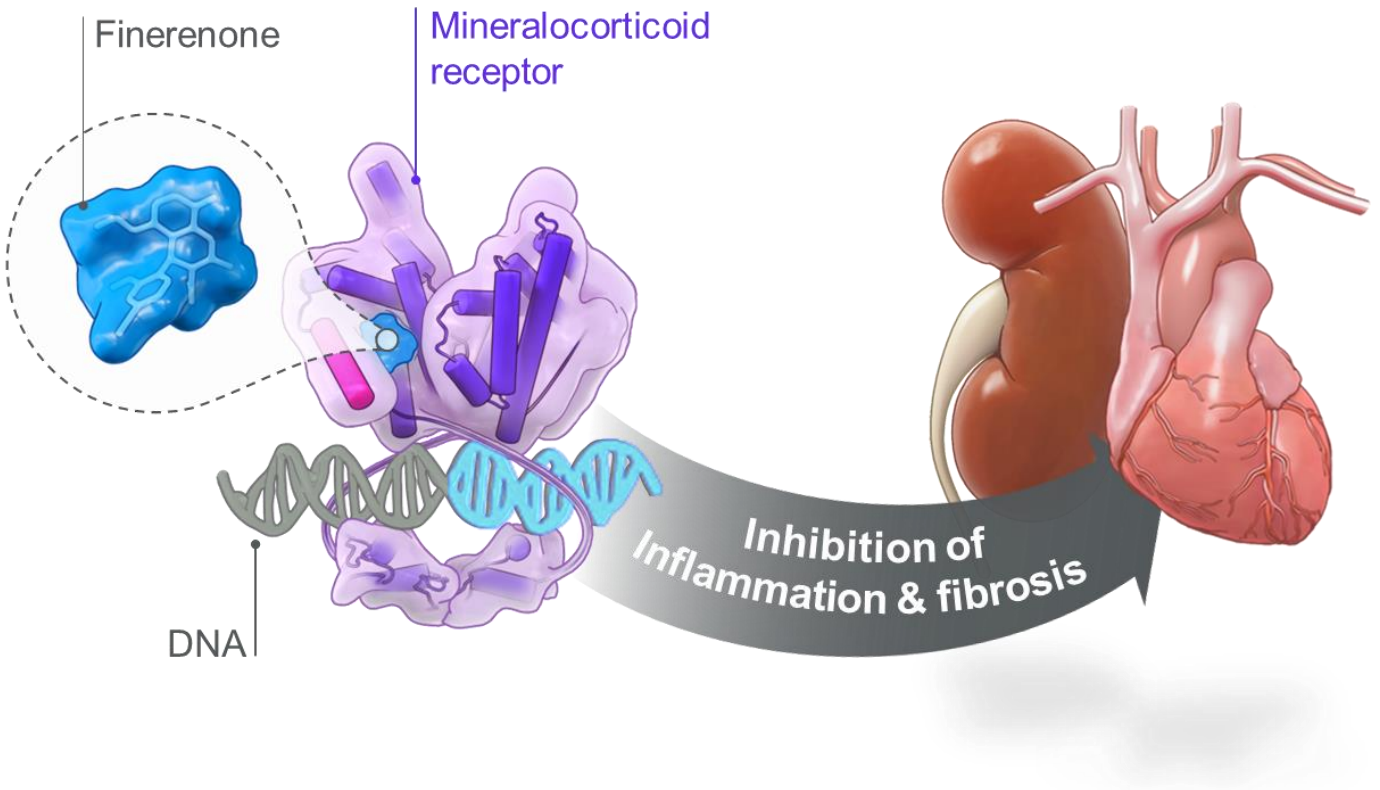
Increasing CKM Overlap in Trials of HFmrEF or HFpEF Over Time



Ostrominski JW…Vaduganathan M. JACC 2024

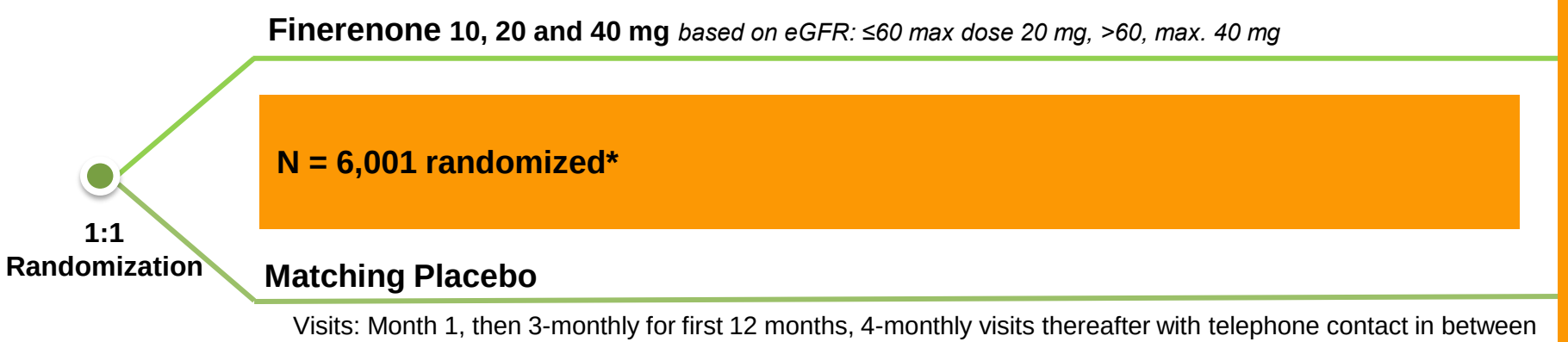
Could the Non-Steroidal MRA, Finerenone, Modify Risk across the CKM Spectrum?

- **Finerenone is a non-steroidal MRA that has been studied in RCTs of patients with T2D and CKD and separately in patients with HF (with and without T2D)**
- **However, none of these trials were individually powered to evaluate treatment effects on cardiovascular mortality**



Design of the FINEARTS-HF Trial

FINEARTS-HF was 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, &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

Vaduganathan M…Solomon SD. EJHF 2024 (in press); Solomon SD…McMurray JJV. EJHF, 2024

Design of the FIDELIO-DKD Trial

13,911 patients enrolled

Run-in[1,2] → Screening

4–16 weeks
Optimisation of ACEi/ARB therapy

5734 patients randomised

R

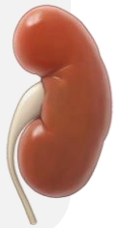
- **Finerenone** (initial dose 10 or 20 mg od) → Post-treatment follow-up
- **Placebo** (initial dose 10 or 20 mg od) → Post-treatment follow-up

2.6 years' median follow-up

Primary endpoint

1. Kidney composite

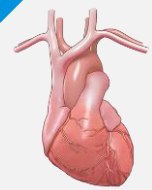
Time to kidney failure, sustained ≥40% decrease in eGFR from baseline, or renal death



Secondary endpoints

2. CV composite

Time to CV death, non-fatal MI, non-fatal stroke or hospitalisation for HF



3. Death from any cause

4. Hospitalization for any cause

5. Change in UACR

6. Second kidney composite

Key eligibility criteria

- T2D
- CKD
- Optimized RASi for ≥4 weeks
- Serum [K+] ≤4.8 mmol/l

- HFrEF with NYHA Class II–IV
- Uncontrolled arterial hypertension

Bakris G, *et al. N Engl J Med* 2020

Design of the FIGARO-DKD Trial

19,381 patients enrolled

Run-in[1,2] → Screening

4–16 weeks
Optimisation of ACEi/ARB therapy

7,437 patients randomised

R

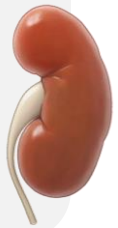
- **Finerenone (initial dose 10 or 20 mg od)** → Post-treatment follow-up
- **Placebo (initial dose 10 or 20 mg od)** → Post-treatment follow-up

3.4 years' median follow-up

Primary endpoint

1. CV composite

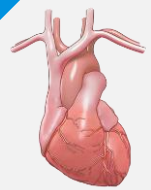
Time to CV death, non-fatal MI, non-fatal stroke or hospitalisation for HF



Secondary endpoints

2. kidney composite

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



3. Hospitalization for any cause

4. Death from any cause

5. Change in UACR

6. Second kidney composite

Key eligibility criteria

- T2D
- CKD
- Optimized RASi for ≥4 weeks
- Serum [K+] ≤4.8 mmol/l

- HFrEF with NYHA Class II–IV
- Uncontrolled arterial hypertension

Pitt B, *et al. N Engl J Med* 2021

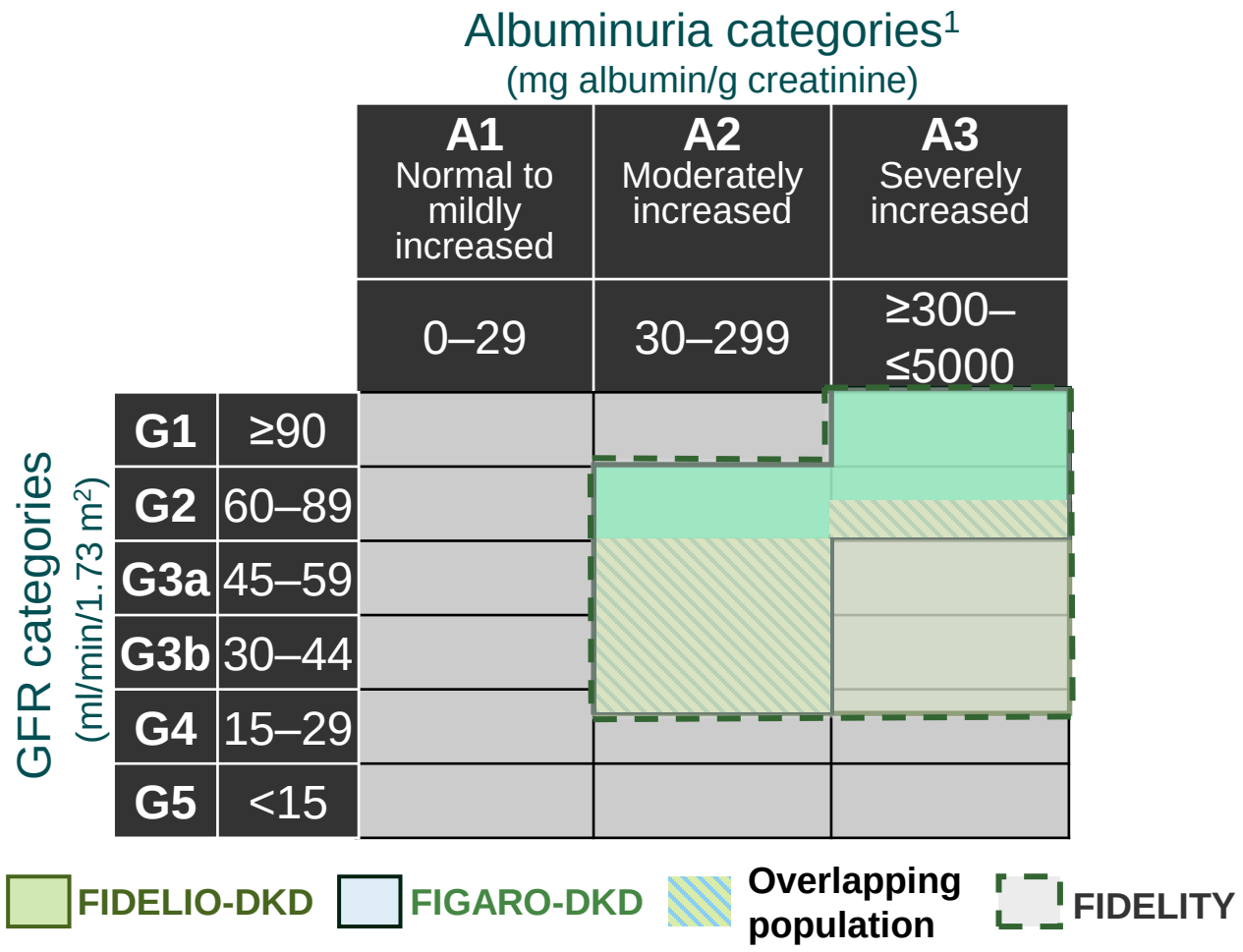
KDIGO Kidney Risk Distribution in FINEARTS-HF

eGFR (mL/min/1.73 m²)			UACR (mg/g) A1 <30	A2 30-300	A3 >300
	G1	≥90	6.3%	2.4%	0.5%
	G2	60-89	28.5%	11.2%	2.8%
	G3a	45-59	15.4%	8.2%	2.6%
	G3b	30-44	8.7%	6.5%	3.0%
	G4	15-29	1.6%	1.2%	0.9%
	G5	<15	0.0%	0.0%	0.0%

KDIGO Risk Categories			
Low	Moderate	High	Very High
34.9%	29.1%	20.2%	15.8%

Ostrominski JW…Vaduganathan M. JCF 2024

KDIGO Kidney Risk Distribution in FIDELIO-DKD and FIGARO-DKD



FIDELITY[4]
N=13,171

FIDELIO-DKD[2]
N=5734

FIGARO-DKD[3]
N=7437

1. Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2020;98:S1–S115; 2. Bakris G, *et al*. NEJM 2020; 3. Pitt B, *et al. N Engl J Med* 2021; 4. Agarwal R, *et al. Eur Heart J* 2021

Design of FINE-HEART Umbrella Program

FINEHEART

(n=19,027 Participants)

FINEARTS-HF

FIDELIO-DKD

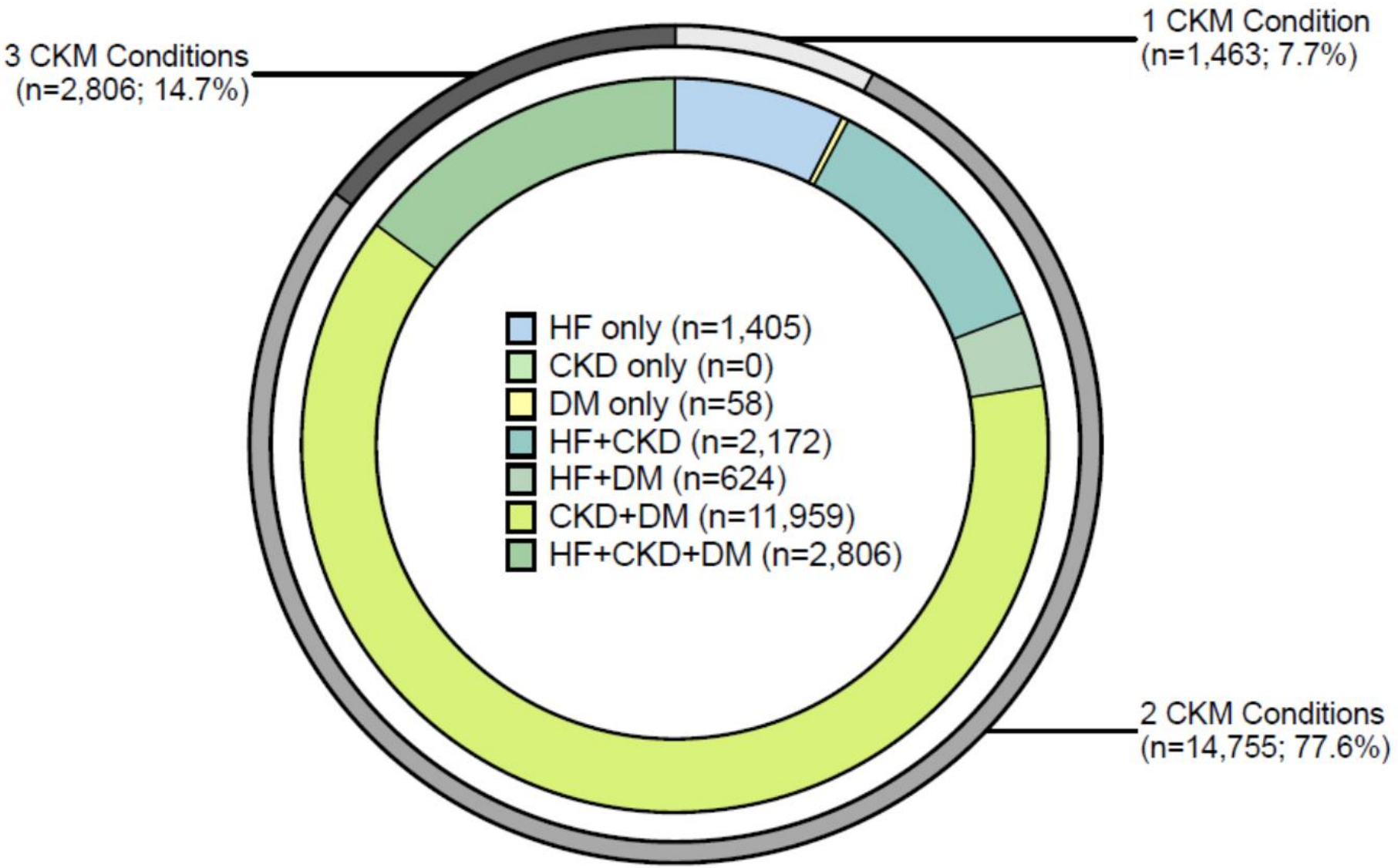
FIGARO-DKD

FINE-HEART will have increased precision to robustly assess the efficacy and safety of the non-steroidal MRA finerenone on CV death and other cardio-kidney outcomes, and will be enriched for participants with a high burden of CKM multimorbidity.

Baseline Characteristics of FINE-HEART Integrated Population (n=19,027)

Age	67±10
Women	35%
BMI (kg/m^2)	31±6
Systolic BP (mmHg)	134±15
eGFR (mL/min/1.73m^2)	59±21
<25	1%
25 to <45	29%
45 to <60	26%
≥60	44%
UACR (mg/g)	640±913
A1: <30	20%
A2: 30 to <300	31%
A3: ≥300	49%
Hemoglobin A1c (%)	7.3±1.4
History of HF	37%
History of Diabetes	81%
History of AF/AFL	25%
Diuretic	63%
ACEi	38%
ARB	56%
SGLT2i	9%

Cardio-Kidney-Metabolic Overlap in FINE-HEART



CKD defined as eGFR<60mL/min/1.73m^2 or UACR≥30mg/g at randomization

Thank you

48 countries, 1024 sites, 13,911* participants

Executive committee

George L. Bakris (Principal Investigator); Gerasimos Filippatos; Rajiv Agarwal; Stefan D. Anker; Luis M. Ruilope; Bertram Pitt

Independent data monitoring committee

Murray Epstein; Aldo Maggioni; Glenn Chertow; Gerald DiBona; Tim Friede; Jose Lopez-Sendon; Jean Rouleau

Clinical event committee

Rajiv Agarwal (Chair); Stefan Anker; Phyllis August; Andrew Coats; Hans Diener; Wolfram Döhner; Barry Greenberg; Stephan von Haehling; James Januzzi; Alan Jardine; Carlos Kase; Sankar Navaneethan; Lauren Phillips; Piotr Ponikowski; Pantelis Sarafidis; Titte Srinivas; Turgut Tatlisumak; John Teerlink

National lead investigators

Augusto Vallejos; Richard MacIsaac; Guntram Schernthaner; Pieter Gillard; Maria Eugenia F. Canziani; Theodora Temelkova-Kurktschiev; Ellen Burgess; Sheldon Tobe; Fernando González; Zhi-Hong Liu; Andrés Ángelo' Cadena Bonfanti; Carlos Francisco Jaramillo; Martin Prazny; Peter Rossing; Jorma Strand; Michel Marre; Roland Schmieder; Christoph Wanner; Pantelis Sarafidis; Juliana Chan; László Rosivall; Joseph Eustace; Ehud Grossman; Yoram Yagil; Giuseppe Remuzzi; Daisuke Koya; Takashi Wada; Magdalena Madero Rovalo; Ron Gansevoort; Adriaan Kooy; Trine Finnes; Froilan De Leon; Janusz Gumprecht; Fernando Teixeira e Costa; Alexander Dreval; Anantharaman Vathsala; Aslam Amod; Sin Gon Kim; Byung Wan Lee; Julio Pascual Santos; Bengt-Olov Tengmark; Michel Burnier; Chien-Te Lee; SukitYamwong; Ramazan Sari; Kieran McCafferty; Borys Mankovsky; Sharon Adler; Linda Fried; Robert Toto; Mark Williams; Tran Quang Khan

FIDELIO-DKD

FInerenone in reducing kiDnEy faiLure and dIsease prOgression in DKD

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

*Number of patients who provided informed consent

Thank you

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

Executive committee
George L. Bakris; Gerasimos Filippatos; Rajiv Agarwal; Stefan D. Anker; Luis M. Ruilope; Bertram Pitt

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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

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

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Clinical Events Committee
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

National Lead Investigators
Subodh Verma, MD, Mikhail Kosiborod, MD
(lead National Lead Investigators)

Argentina	**Felipe Martinez**
Australia	**J. Atherton**
Austria	**Dirk von Lewinski**
Brazil	**Jose Francisco Kerr Saraiva**
Bulgaria	**Tzvetana Katova**
Canada	**S. Zeiroth**
Canada	**J.A. Udell**
Canada	**S. Verma as NL coordinator**
China	**Ma chang-sheng**
Colombia	**Clara Inés Saldarriaga**
Czech Rep	**Vojtěch Melenovský**
Denmark	**Morten Schou**
Finland	**Heikki Ukkonen**
Germany	**Johann Bauersachs**
Greece	**G. Filipapatos**
Hungary	**Bela Merkely**
Hong Kong	**Alex Lee**
India	**V. Chopra**
Israel	**Sorel Goland**
Italy	**Savina Nodari**

Japan	**N. Sato**
Latvia	**G. Latkovskis**
Malaysia	**Imran Zainal Abidin**
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Netherlands	**G. Linssen**
New Zealand	**R. Troughton**
Poland	**Grzegorz Gajos.**
Portugal	**Cândida Fonseca**
Romania	**Ovidiu Chioncel**
Russia	**V. Y. Mareev**
Slovakia	**Eva Goncalvesova**
South-Korea	**Seokmin Kang**
Spain	**Josep Comin Colet**
Taiwan	**Chern-En Chiang**
Turkey	**Mehmet Birhan Yılmaz**
UK	**Mark Petrie**
Ukraine	**Leonid Voronkov**
US	**O. Vardeny**
US	**K. Sharma**
US	**M. Kosiborod**

We thank all the FINEARTS-HF Investigators and participants!