



17-20  
Dicembre  
2025  
Napoli

70° CONGRESSO  
NAZIONALE  
**SIGG**  
LIBERI E LONGEVI

Università degli  
Studi di Napoli  
Federico II  
Polo Didattico  
di **SCAMPIA**



SOCIETÀ ITALIANA  
DI GERONTOLOGIA  
E GERIATRIA

---

## Finerenone nel trattamento dell'HFpEF

---

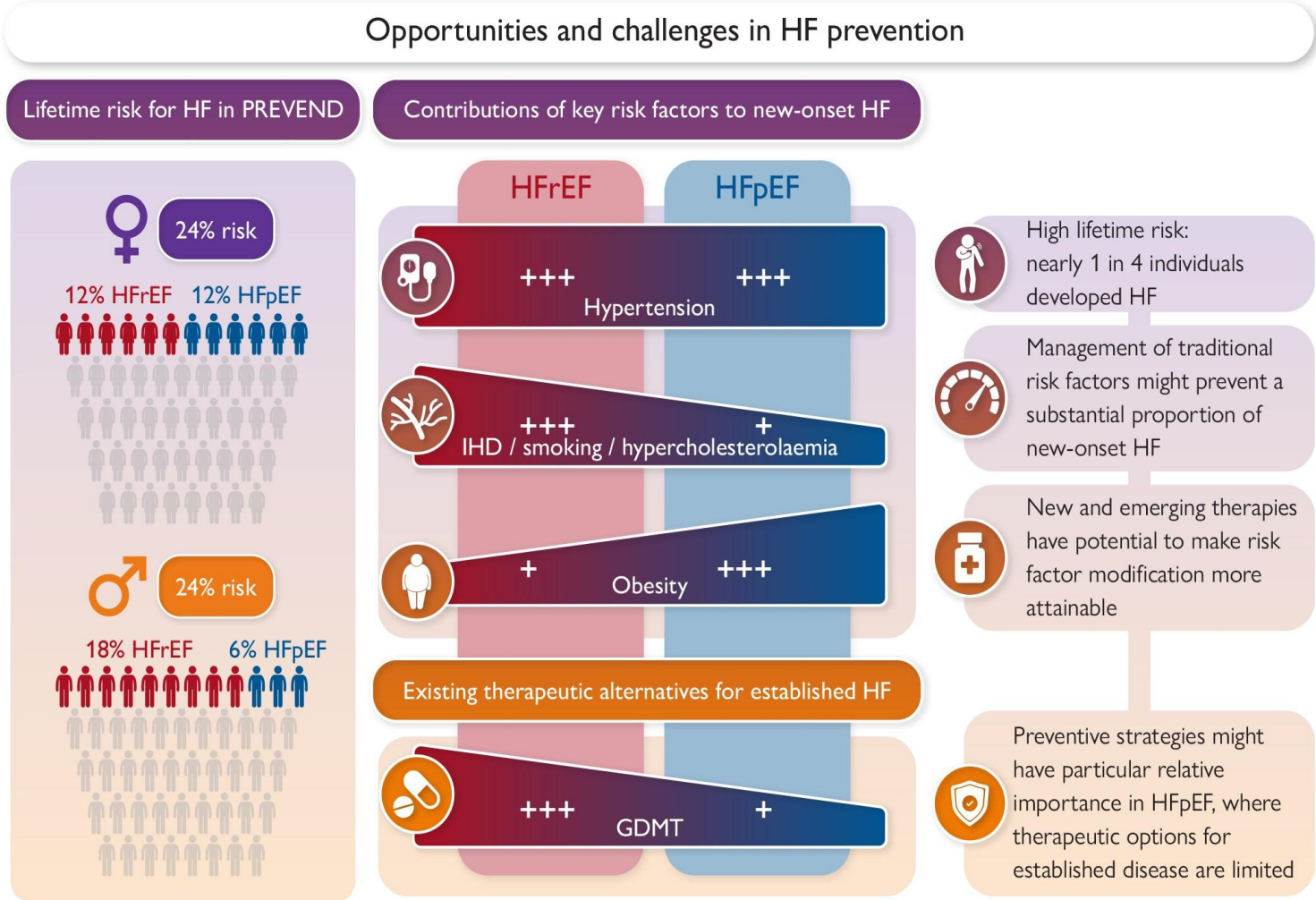
### Giuseppe Rengo, MD, PhD



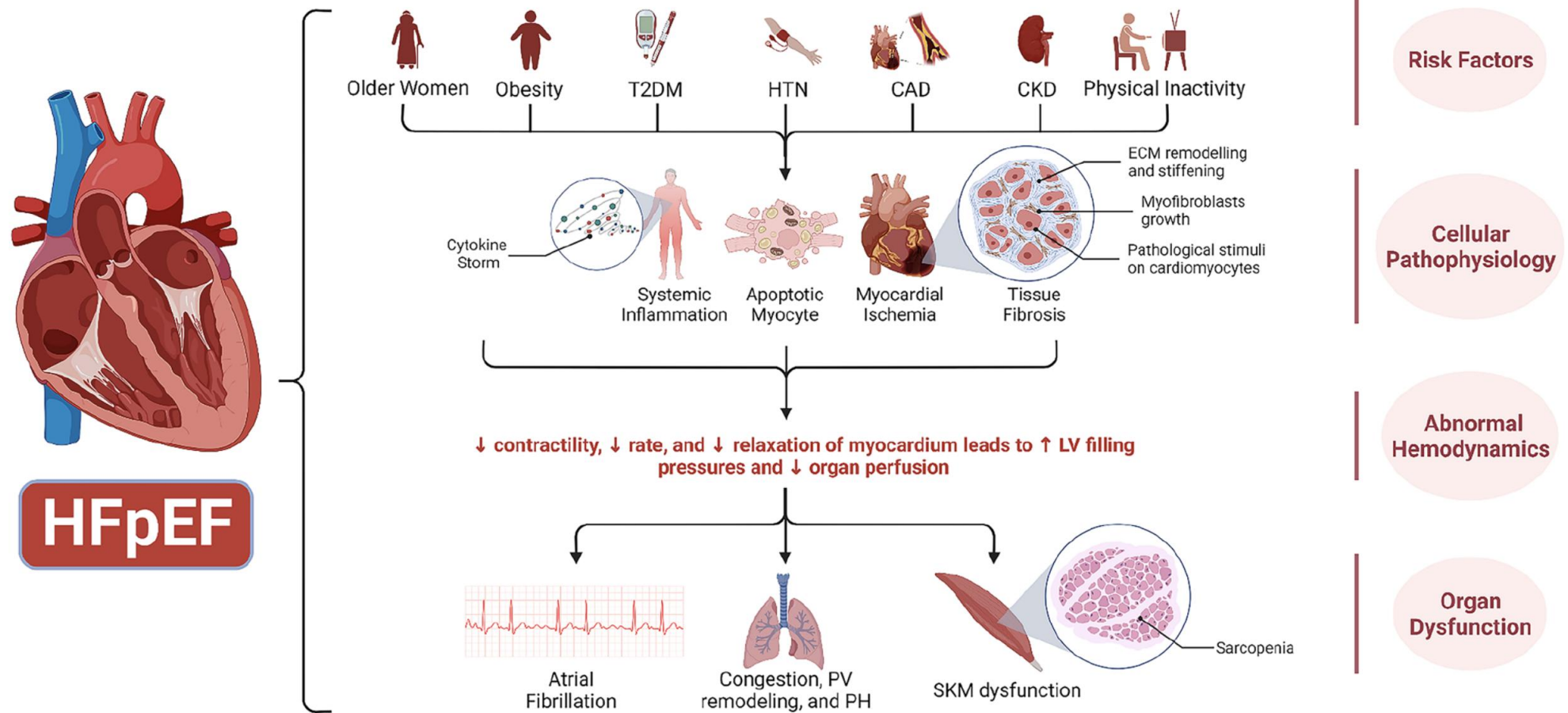
Professore Ordinario di Geriatria  
Dipartimento di Scienze Mediche Traslazionali  
Università degli Studi di Napoli Federico II

Direttore U.O.C. di Geriatria e Fibrosi Cistica dell'Adulto  
D.A.I. Medicina Interna e della Complessità Clinica  
A.O.U. Federico II

# Opportunities and challenges in HF

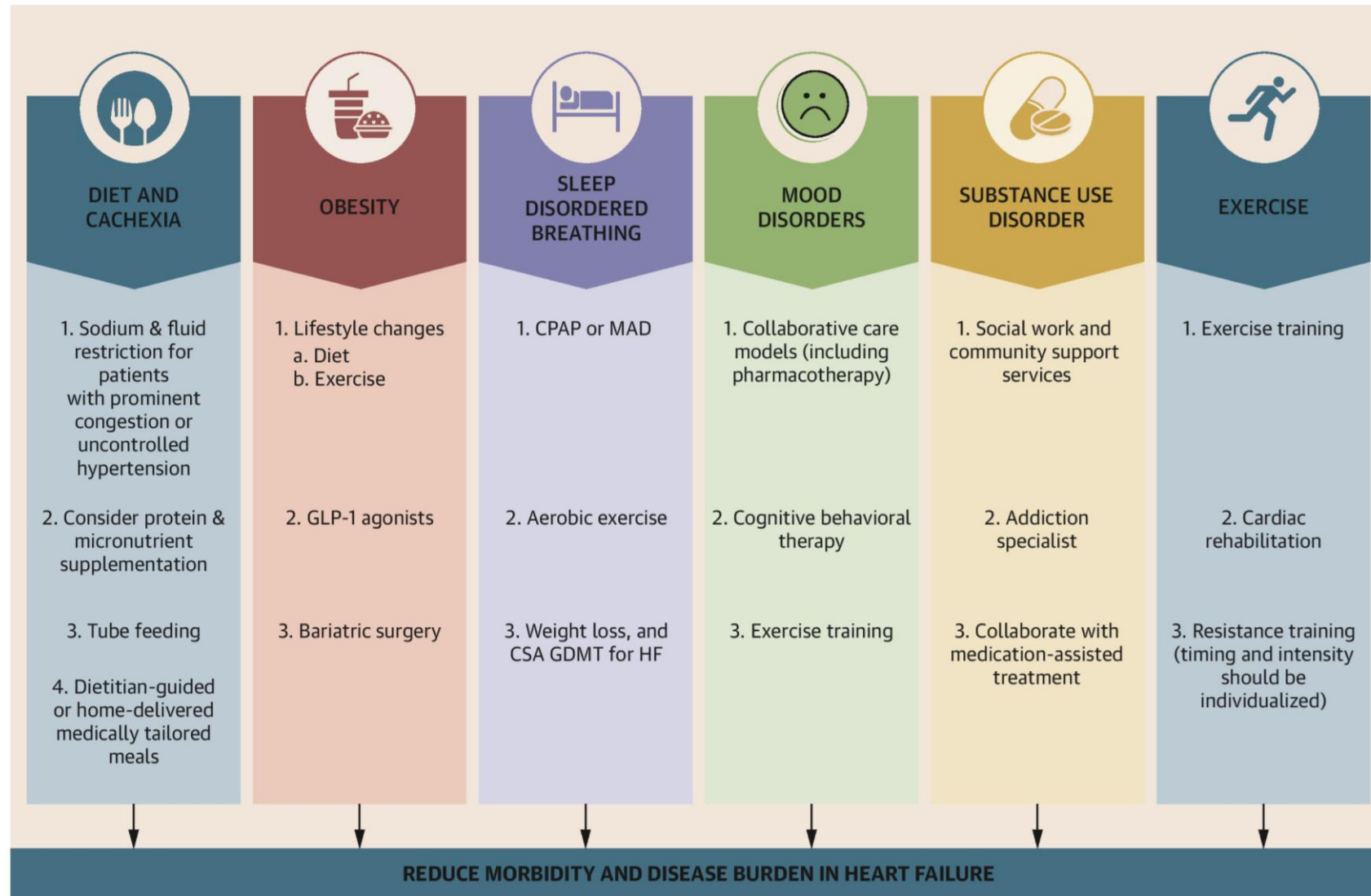


# HFpEF is a part of a complex and systemic disease

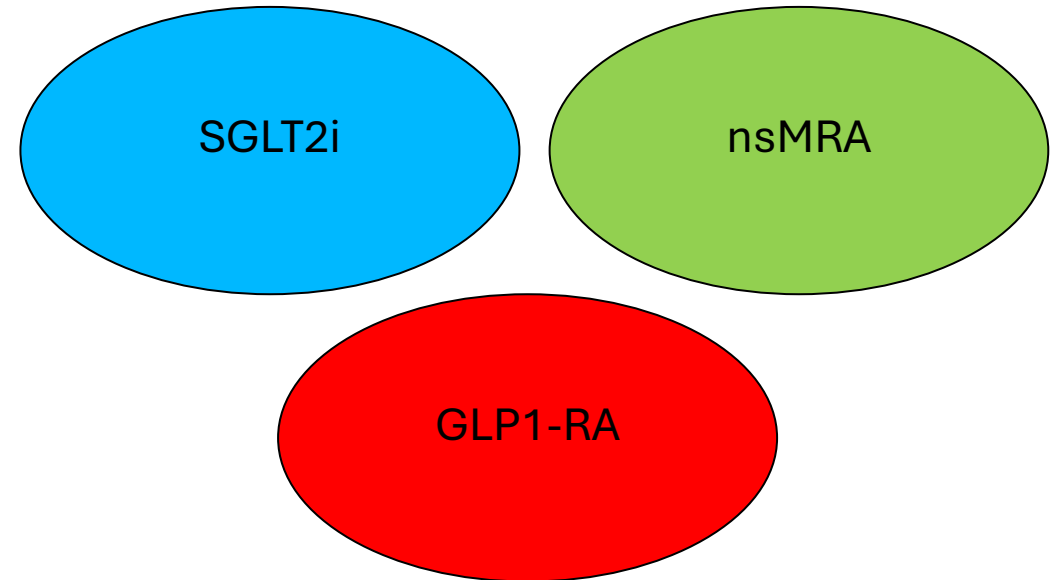
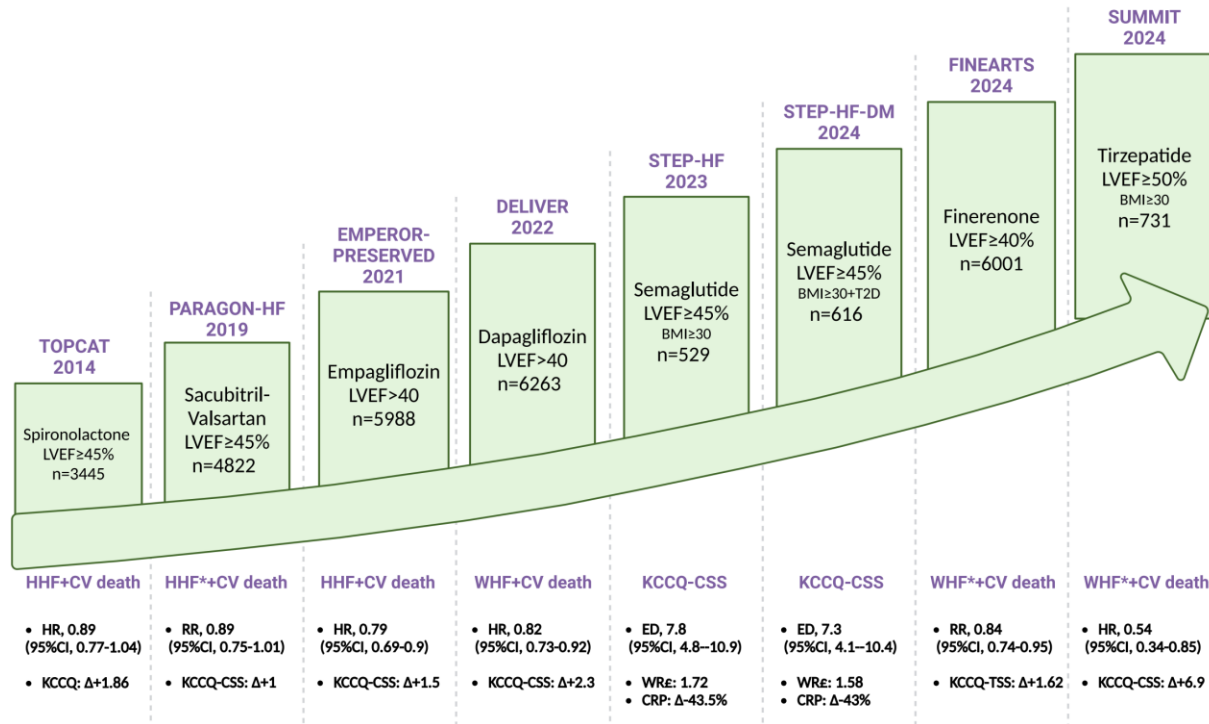


# HFpEF Management: Nonpharmacological treatments

## *comorbidities management*



# HFpEF treatments: The Pillars



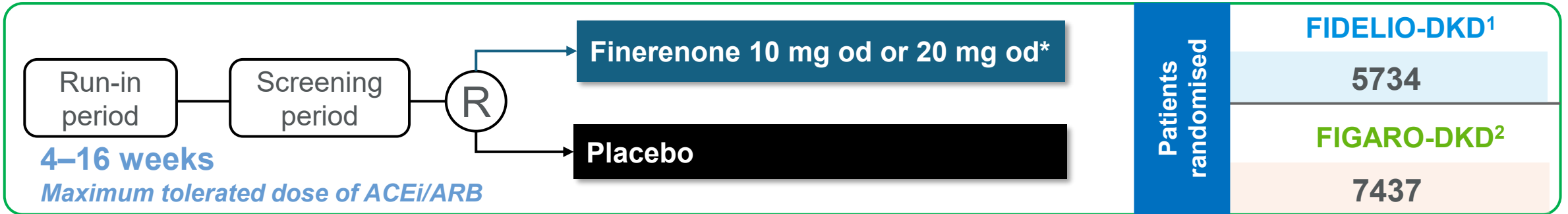
# Differential MR binding of steroidal MRAs vs finerenone results in distinct effects on gene expression

	Steroidal aldosterone antagonists		
	Spironolactone	Eplerenone	Finerenone
<b>Structural properties</b>	Flat (steroidal)	Flat (steroidal)	Bulky (nonsteroidal)
<b>Potency to MR</b>	High	Moderate	High
<b>Selectivity to MR</b>	Low	Moderate	High
<b>Half-life</b>	>20 hours*	4–6 hours*	2–3 hours
<b>Active metabolites</b>	++	–	–
<b>CNS penetration</b>	Yes	Yes	No based on preclinical data
<b>Gynecomastia</b>	Yes	Less than spironolactone	No signal in phase II studies
<b>Hyperkalaemia</b>	Yes	Yes <sup>4</sup>	Moderately increased*
<b>Tissue distribution</b>	Kidney > heart (at least 6-fold)	Kidney > heart (~3-fold)	Balanced kidney : heart (1:1)
<b>Indication (SmPC)</b>	Congestive HF <sup>2</sup>	HF and LVEF ≤40% or ≤30%	CKD with albuminuria associated with T2D

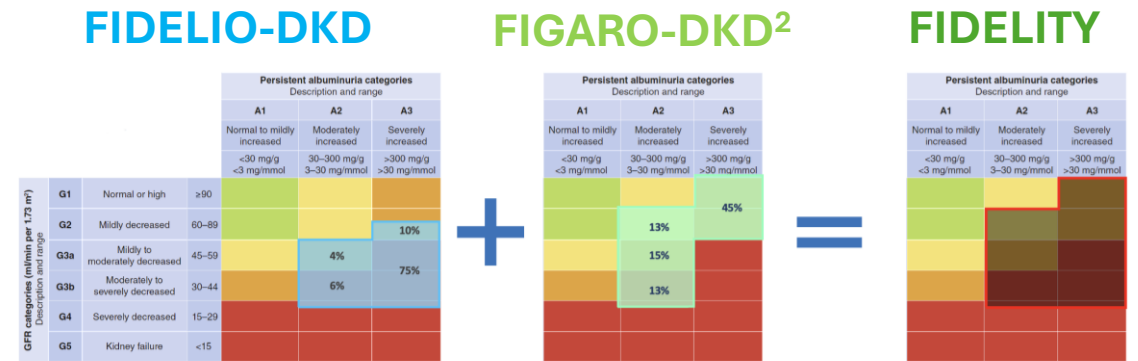
Based on preclinical data and ARTS phase II programme

- Non-steroidal MRAs are pharmacologically distinct from classical MRAs with a unique structure;
- Higher affinity and specificity for the mineralocorticoid receptor, no sexual side effects;
- Highly potent: increased anti-inflammatory and antifibrotic actions;
- Different distribution with greater and balanced tropism for cardiac and renal receptors;
- Better safety profile: lower rate of hyperkalaemia.

# Evidences supporting Finerenone cardio-renal benefits: FIDELITY prespecified pooled analysis of landmark trials FIDELIO-DKD and FIGARO-DKD



	FIDELIO-DKD <sup>1</sup>	FIGARO-DKD <sup>2</sup>
<b>Clinical efficacy primary endpoint</b>	<b>Composite endpoint:</b> time to onset of kidney failure* or decrease of eGFR $\geq 40\%$ from baseline or death due to kidney disease	<b>Composite endpoint:</b> time to CV death, non-fatal MI, non-fatal stroke or hospitalisation for HF
<b>Key secondary endpoints</b>	Same as primary endpoint in FIGARO-DKD	Same as primary endpoint in FIDELIO-DKD
<b>Enrolled patients</b>	5734 patients with: <ul style="list-style-type: none"> <li>• ACR 30-300 mg/g and eGFR 25-60 mL/min/1.73 m<sup>2</sup>.</li> <li>• ACR 300-5000 and eGFR 25-75 mL/min/1.73 m<sup>2</sup>.</li> </ul>	7437 patients with: <ul style="list-style-type: none"> <li>• ACR 30-300 mg/g and eGFR 25-90 mL/min/1.73 m<sup>2</sup>.</li> <li>• ACR 300-5000 and eGFR &gt;60 mL/min/1.73 m<sup>2</sup>.</li> </ul>

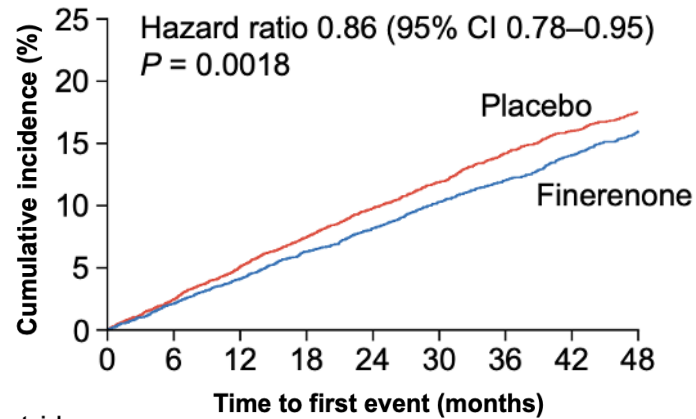


In FIDELITY, 40% of pts. were diagnosed with CKD based on albuminuria criteria (eGFR > 60%)

# Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis

## CV composite

Time to CV death, non-fatal MI, non-fatal stroke or HFrEF



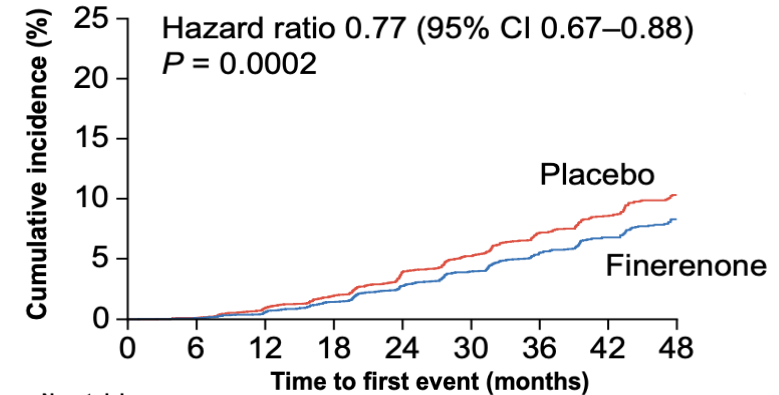
No. at risk	0	6	12	18	24	30	36	42	48
Placebo	6507	6330	6125	5938	5184	4147	2969	2135	1082
Finerenone	6519	6360	6202	6009	5273	4207	3065	2187	1087

**14%** reduced risk of CV morbidity and mortality (HR=0.86; 95% CI 0.78–0.95;  $p=0.002$ )<sup>1</sup>

**22%** reduced risk of HF hospitalization

## Kidney composite

Time to kidney failure, sustained >57% decrease in GFR rate from baseline or renal death

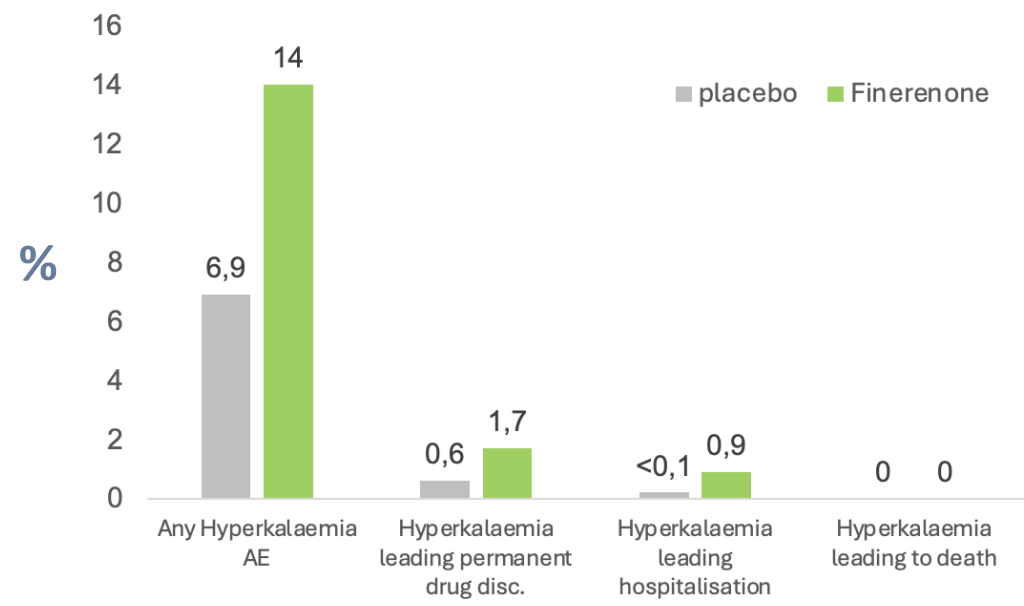
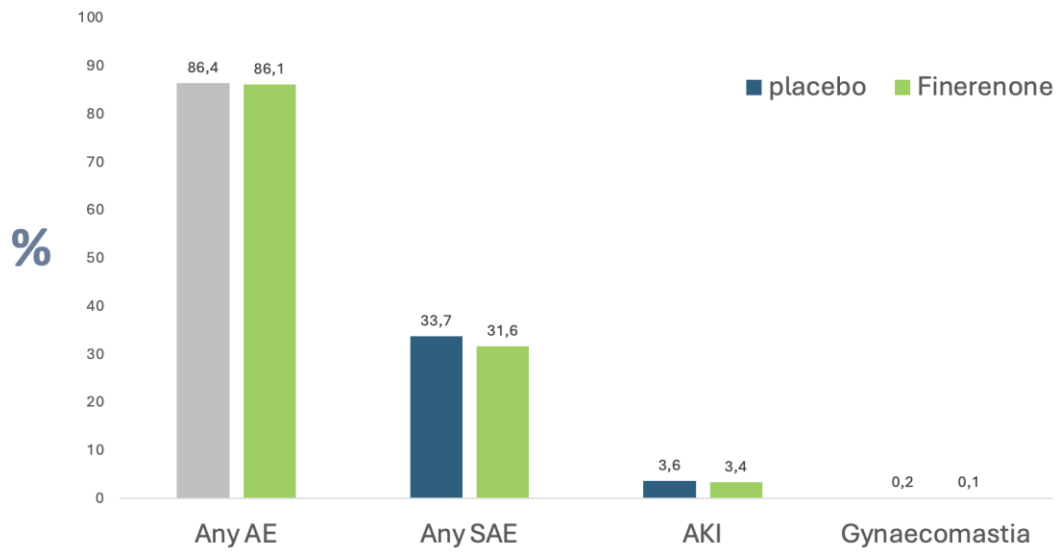


No. at risk	0	6	12	18	24	30	36	42	48
Placebo	6507	6292	6071	5815	4949	3932	2798	1988	962
Finerenone	6519	6291	6107	5848	5027	3973	2815	2024	959

**23%** reduced risk of CKD progression<sup>#</sup> (HR=0.77; 95% CI 0.67–0.88;  $p=0.0002$ )<sup>1</sup>

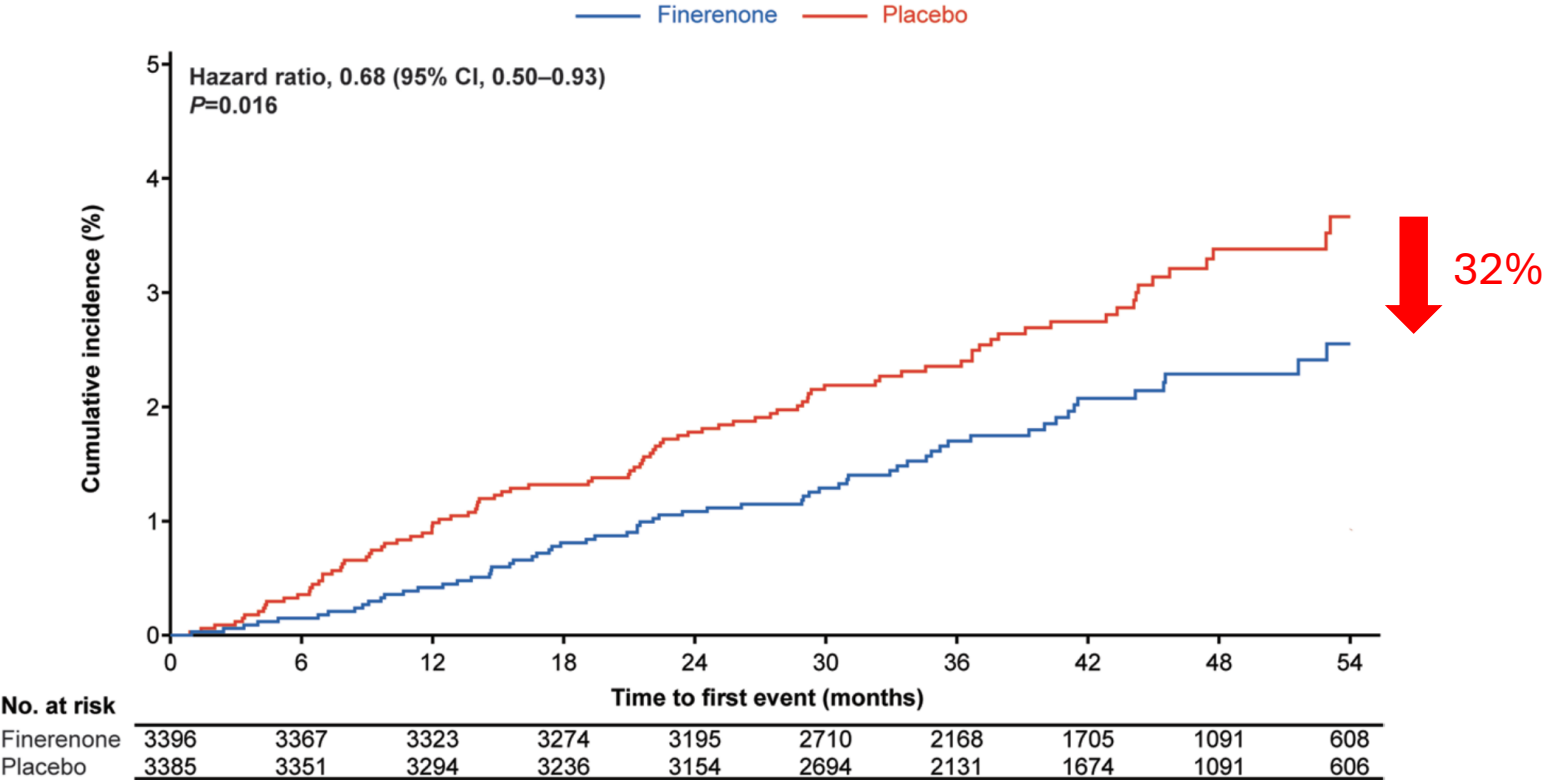
**20%** reduced risk of Dialysis

# Finerenone had similar Adverse Effects compared to placebo and increased incidence of hyperkalaemia, but the clinical impact was minimal

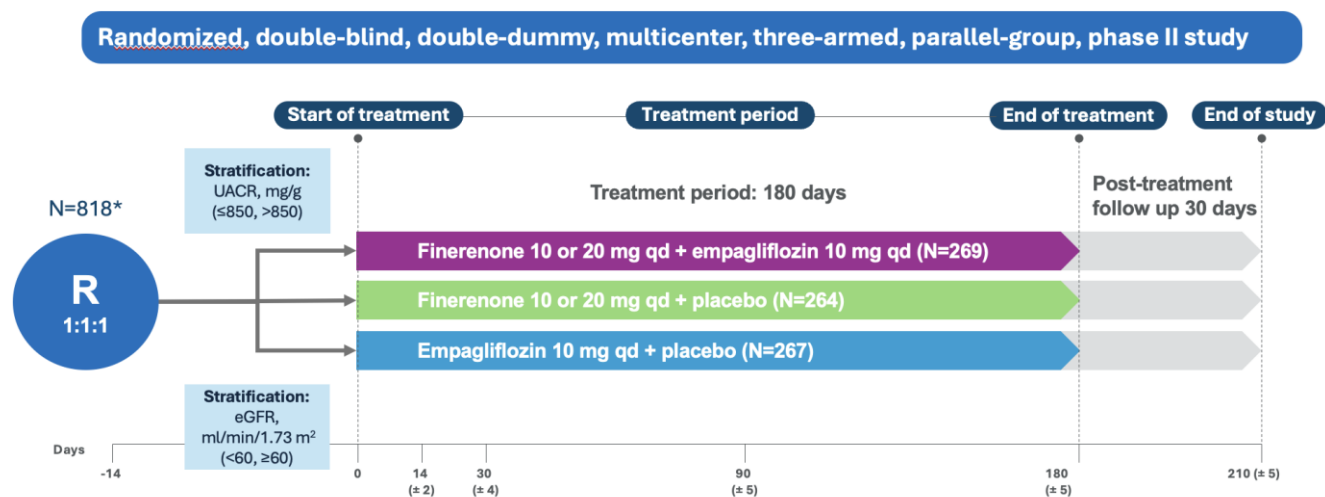


# Figaro-DKD: Finerenone significantly reduced the risk of new-onset HF

Time to new-onset HF in patients without a history of HF at baseline



# CONFIDENCE Trial: efficacy and safety of simultaneous initiation of finerenone and SGLT2i in CKD and T2D Patients



## Primary endpoint

Relative change in UACR from baseline to Day 180:

- Combination versus empagliflozin
- Combination versus finerenone

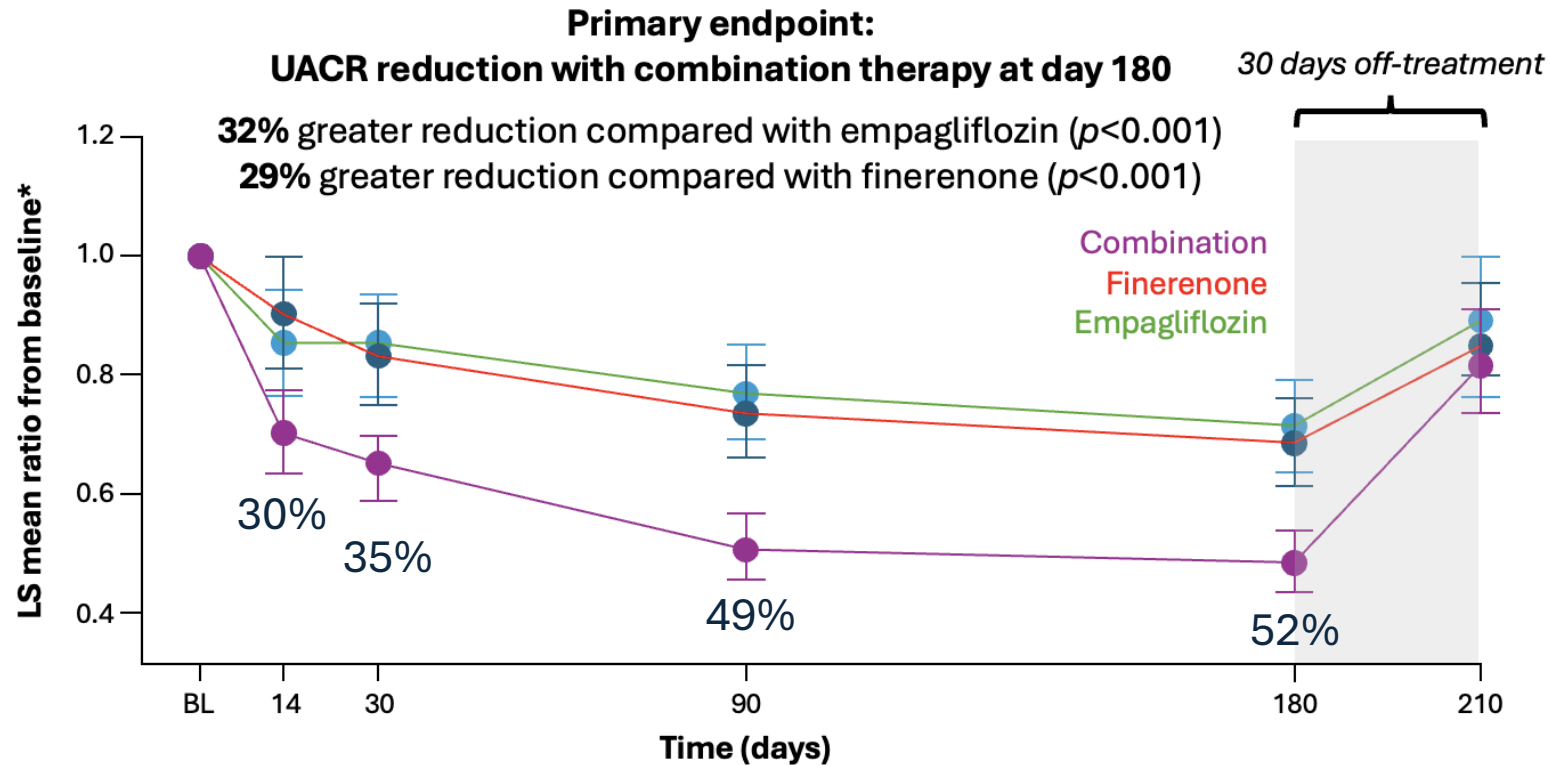
## Secondary safety endpoints

- Initial and longer-term changes in eGFR
- Acute kidney injury
- Treatment-related AEs: hyperkalemia, symptomatic hypotension, genital mycotic events

## Eligibility criteria

- eGFR 30–90 mL/min/1.73m<sup>2</sup>\*
- UACR  $\geq 100$ – $< 5000$  mg/g
- T2D with HbA1c  $< 11\%$
- Exclusion: serum K  $> 4.8$  mmol/L

# Simultaneous initiation of finerenone and an SGLT-2i led to an additive reduction in UACR of up to 52% in patients with CKD and T2D



Neither agent, alone or in combination, led to unexpected adverse events. Symptomatic hypotension, acute kidney injury, and hyperkalemia leading to drug discontinuation were uncommon.

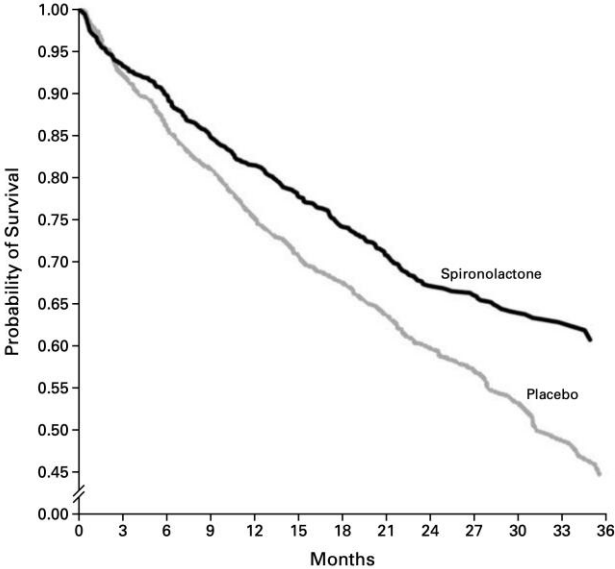
# Recommendations for the prevention of heart failure in patients with type 2 diabetes mellitus and chronic kidney disease

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
In patients with T2DM and CKD, <sup>c</sup> SGLT2 inhibitors are recommended to reduce the risk of HF hospitalization or CV death. <sup>35</sup>	<b>I</b>	<b>A</b>
In patients with T2DM and CKD, <sup>c</sup> finerenone is recommended to reduce the risk of HF hospitalization. <sup>10,11,34,40</sup>	<b>I</b>	<b>A</b>

© ESC 2023

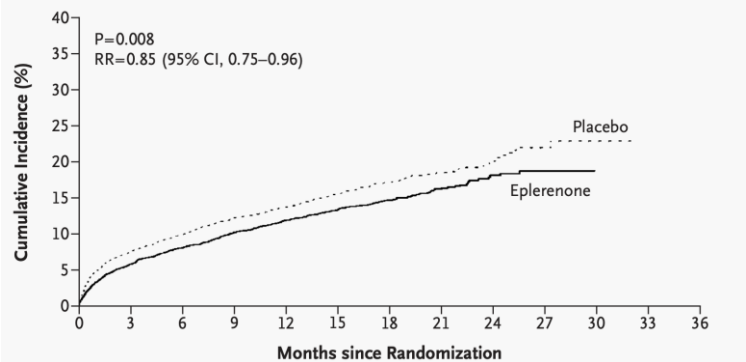
# Steroidal MRA: Benefits in HFrEF

**RALES**  
(severe HFrEF)  
30% Risk reduction



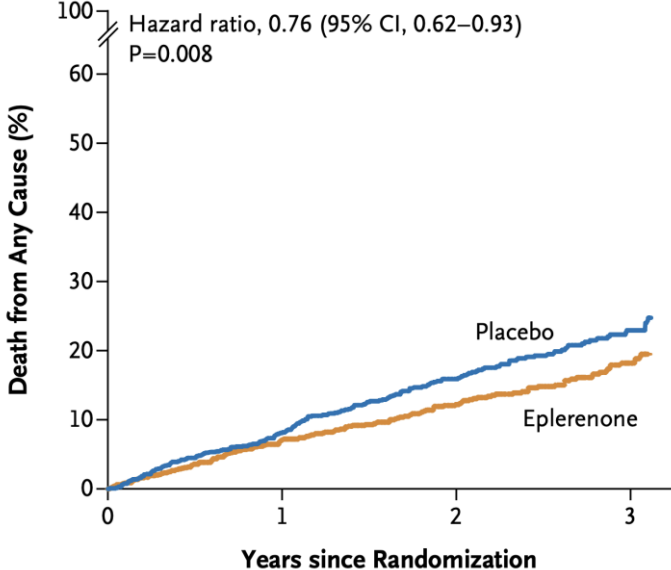
*Pitt B et al. New Engl J Med 1999*

**EPHESUS**  
(post-MI)  
15% Risk reduction



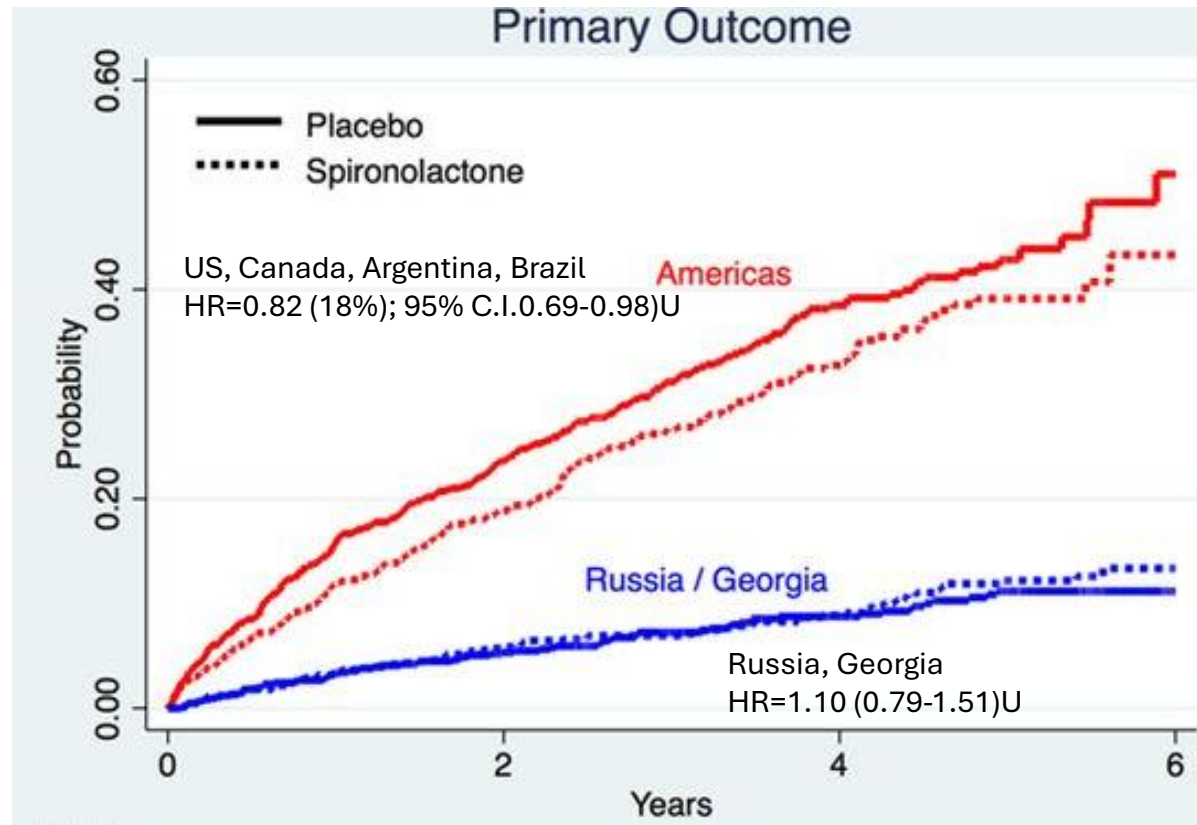
*Pitt B et al. New Engl J Med 2023*

**EMPHASIS**  
(MILD HFrEF)  
24% Risk reduction



*Zannad F et al. New Engl J Med 2011*

# Steroidal MRA: uncertainty in HFmrEF and HFpEF



Time to CV death, aborted cardiac arrest, or HF hospitalization

TOPCAT patients with HFpEF (LVEF  $\geq 45\%$ ) assigned to spironolactone did not achieve a significant reduction in the primary composite outcome compared with patients receiving placebo (despite a reduction in HF hospitalization).

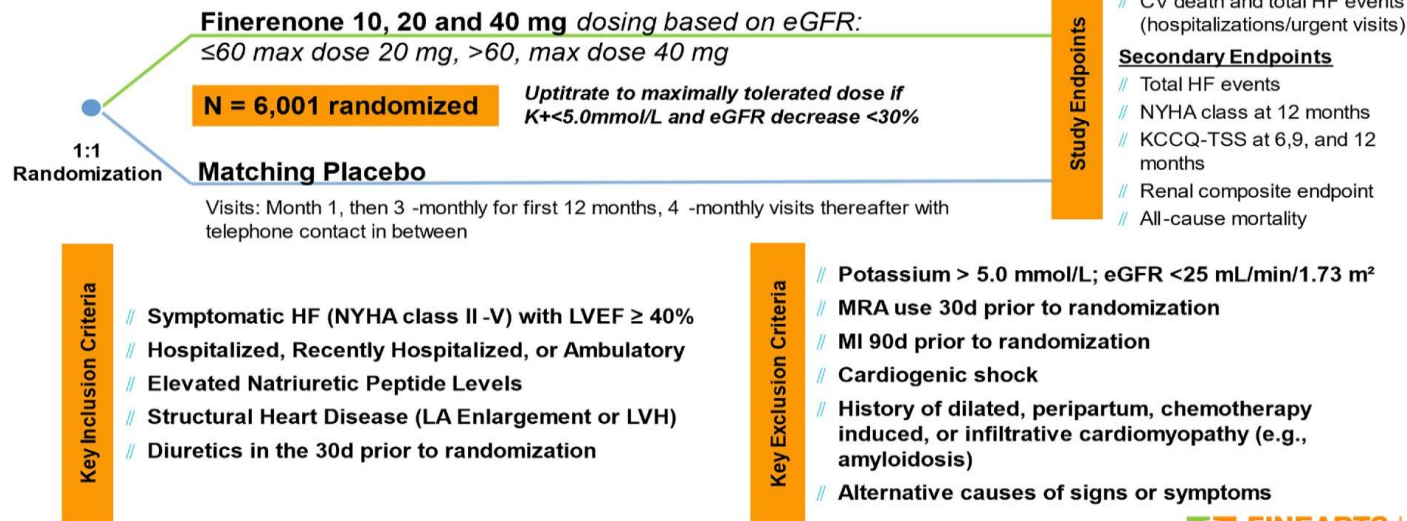
In a post hoc analysis,  $\approx 4$ -fold difference was identified in this composite event rate between the 1678 patients randomized from Russia and Georgia compared with the 1767 enrolled from the United States, Canada, Brazil, and Argentina (the Americas).

# HFpEF Management: Nonpharmacological treatments

## comorbidities management

### FINEARTS-HF Study Design

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

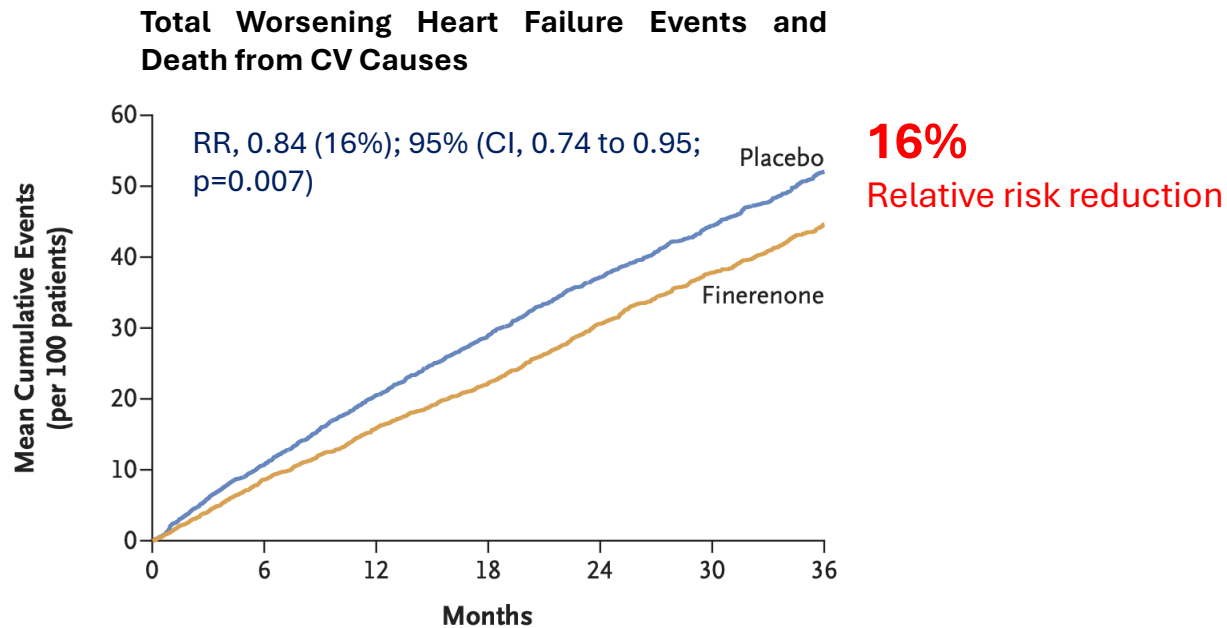


Randomized, double-blind, placebo control trial, testing the hypothesis that finerenone (at a maximum dose of 20 mg or 40 mg once daily) CV death and total worsening HF events in HFpEF patients with a LVEF of 40% or greater .



# Finerenone in HFmrEF and HFpEF: FINEARTS-HF

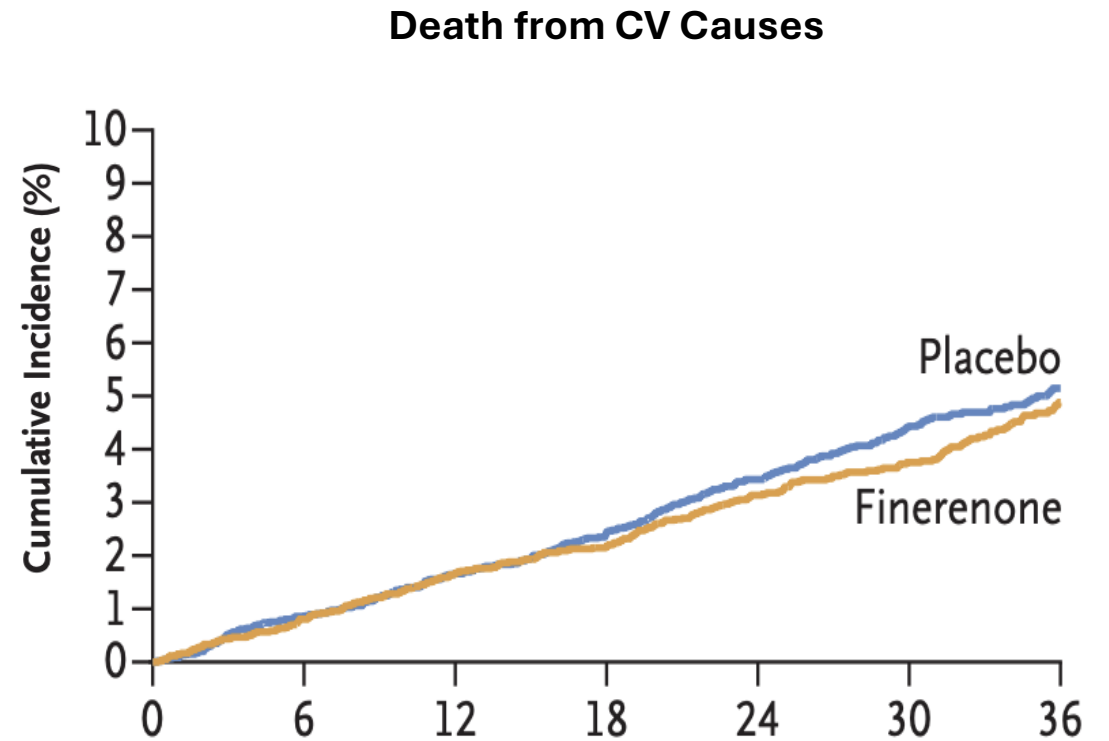
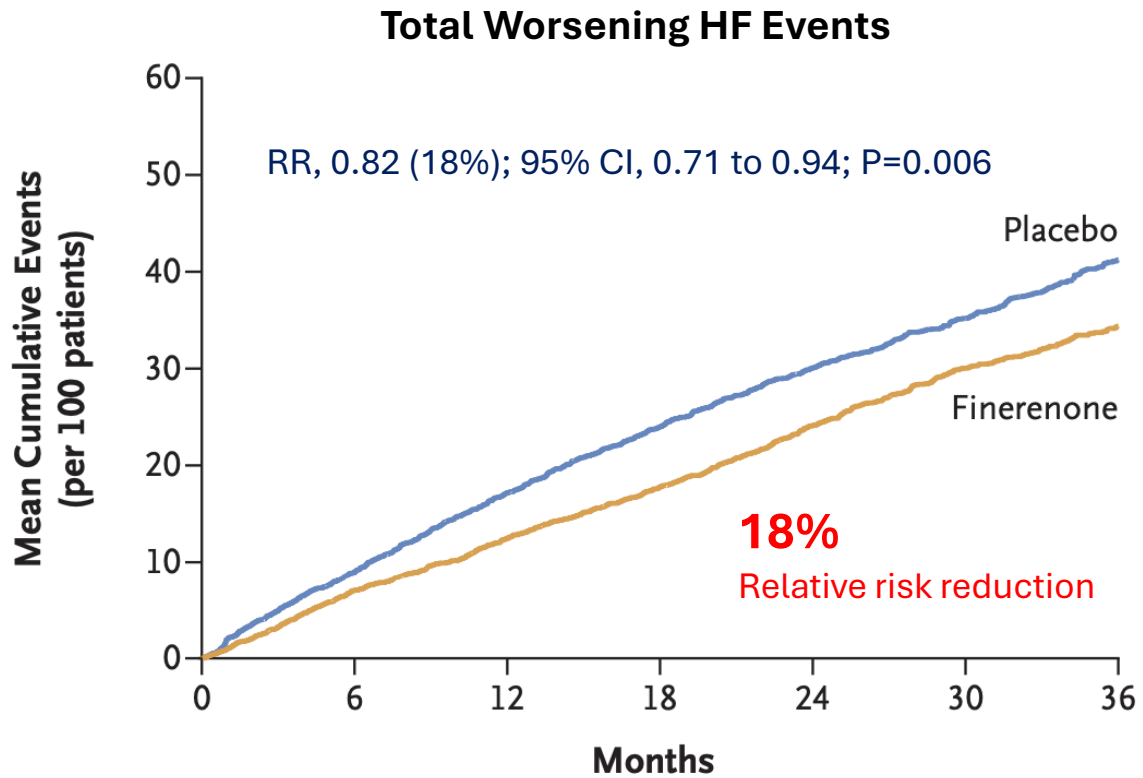
Double-blind trial, 6001 patients with HF and a LVEF of 40% or greater were randomly assigned to receive finerenone (at a maximum dose of 20 mg or 40 mg once daily) or matching placebo, in addition to usual therapy. Median follow-up 2.6 years.



Finerenone resulted in a significantly lower rate of a composite of total worsening HF events and death from CV causes than placebo.

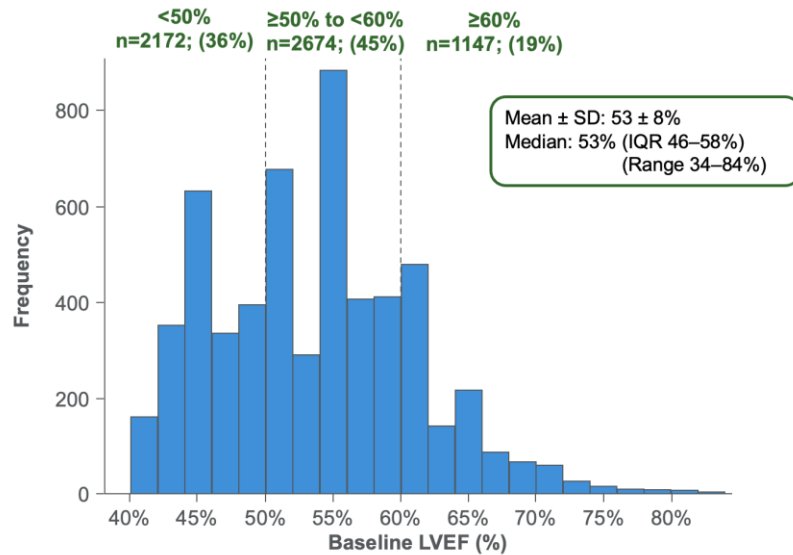
Differences were observed early and remained consistent throughout FINEARTS-HF

# Finerenone in HFmrEF and HFpEF: FINEARTS-HF



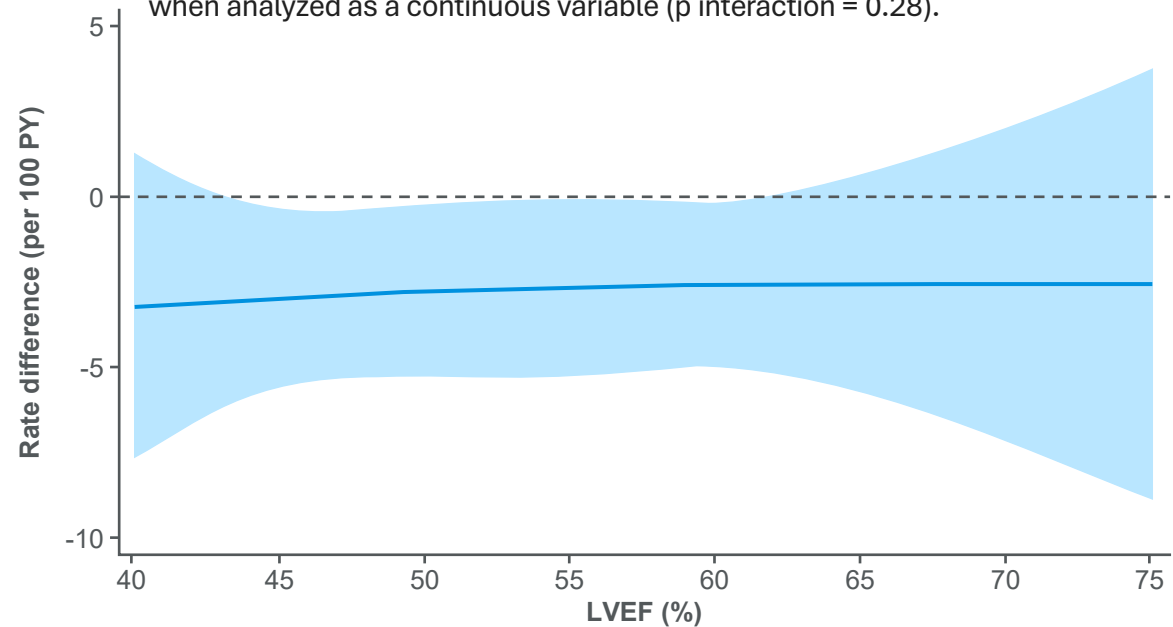
# The absolute benefit of Finerenone versus placebo on the primary endpoint was consistent across the LVEF spectrum

### Distribution of LVEF at baseline in FINEARTS-HF

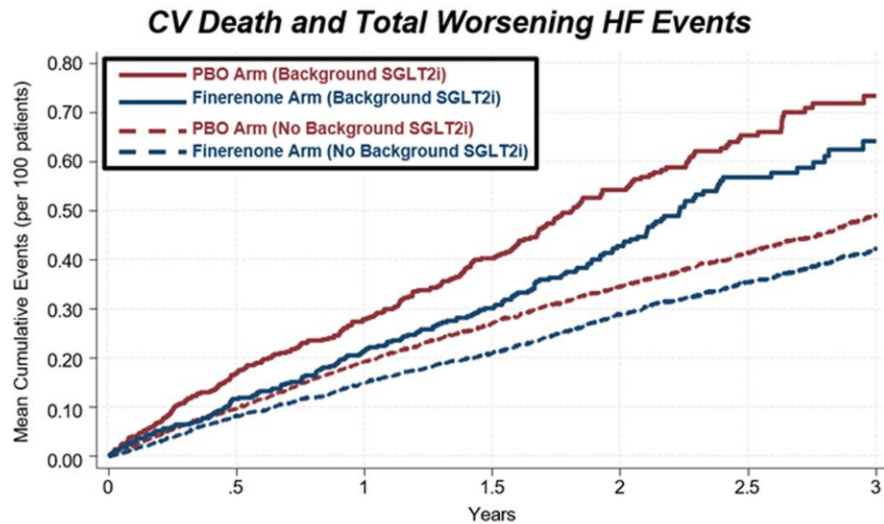


### CV death and total HF events

There was no modification of the benefit of finerenone across the range of LVEF when analyzed as a continuous variable (p interaction = 0.28).



# nsMRA + SGLT2i additive benefits in HFpEF



**SGLT2i Subgroup (n=817):**  
RR 0.83; 95% CI 0.60-1.16  
ARR 4.7 per 100py

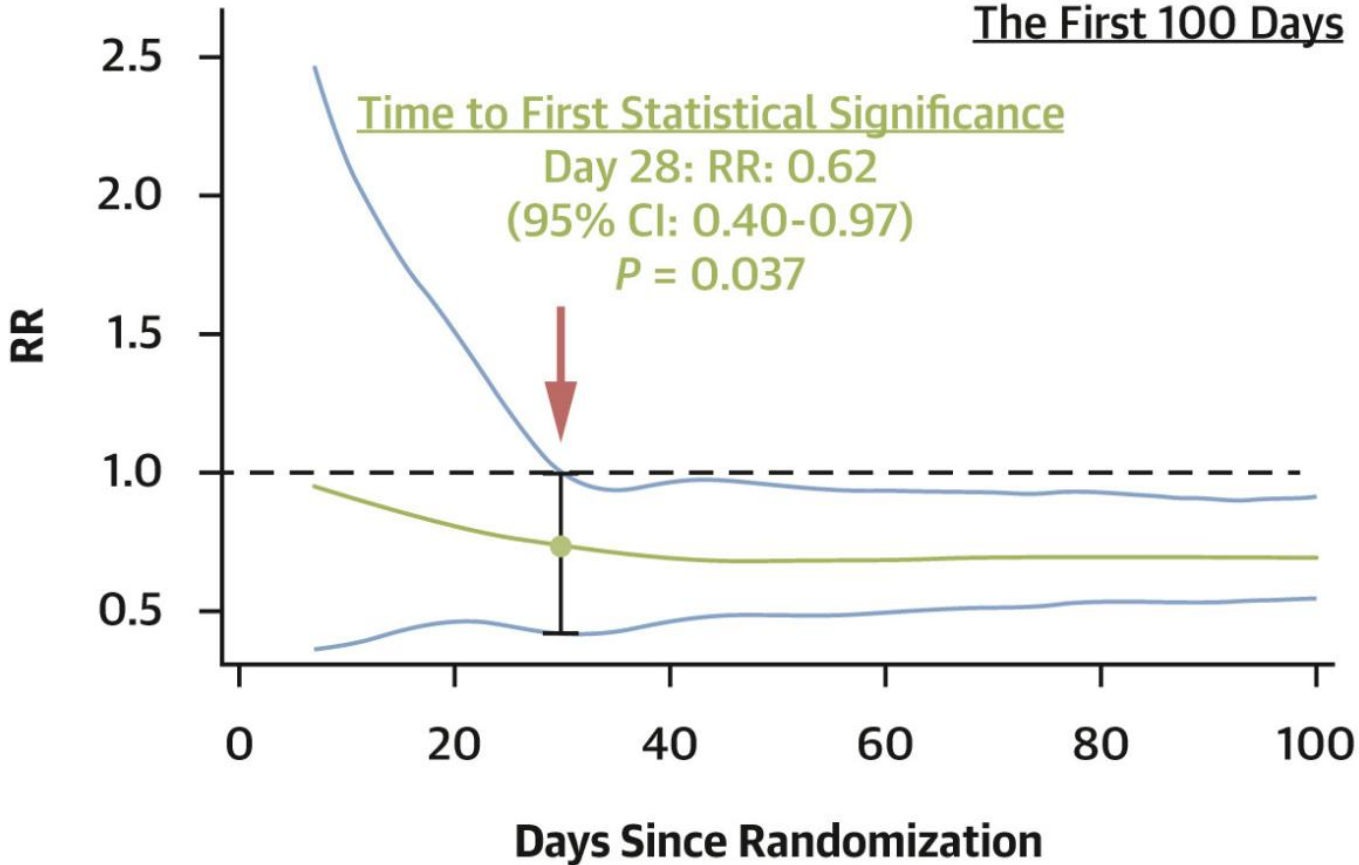
**No SGLT2i Subgroup (n=5,184):**  
RR 0.85; 95% CI 0.74-0.98  
ARR 2.5 per 100py

$p_{\text{interaction}} = 0.76$

Among 6,001 participants, 817 (13.6%) were treated with an SGLT2i at baseline. In follow-up, 980 participants initiated SGLT2i, which was less frequent in the finerenone arm compared with placebo (17.7% vs. 20.1%; HR 0.86; CI 0.76 to 0.97). Time-updated analyses accounting for baseline and subsequent use of SGLT2i did not meaningfully alter the treatment effects of finerenone on the primary endpoint.

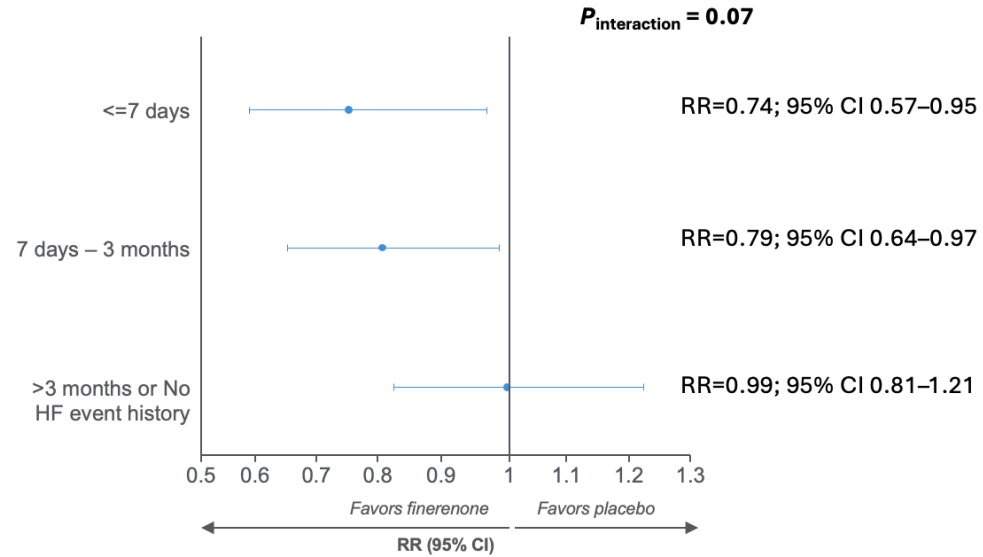
The treatment benefits of the non-steroidal MRA finerenone were observed irrespective of concomitant use of an SGLT2i.

# Time to Significant Benefit of Finerenone in Patients With Heart Failure

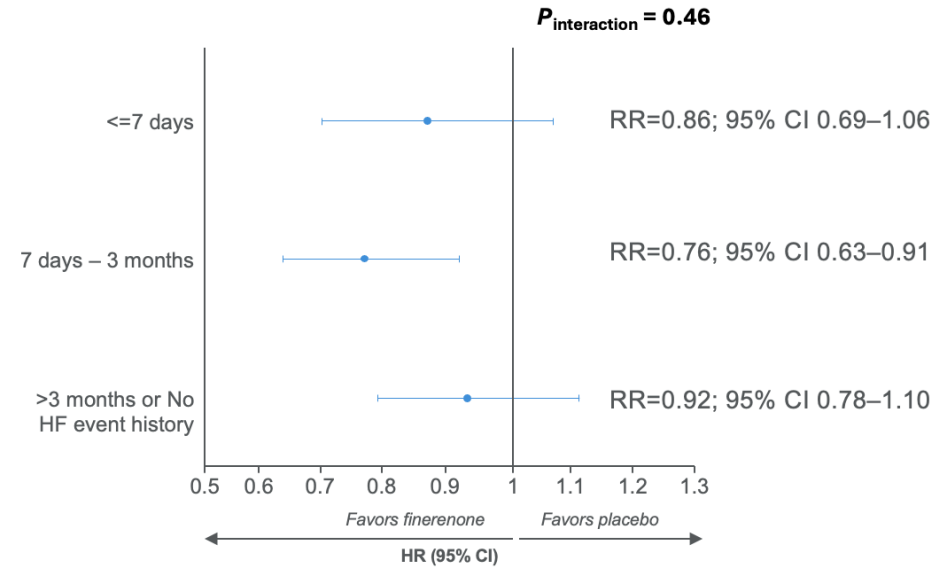


# The absolute treatment effect of finerenone on the primary endpoint appeared to be greater in those with a recent HF event

Primary composite outcome: total HF events and CV death

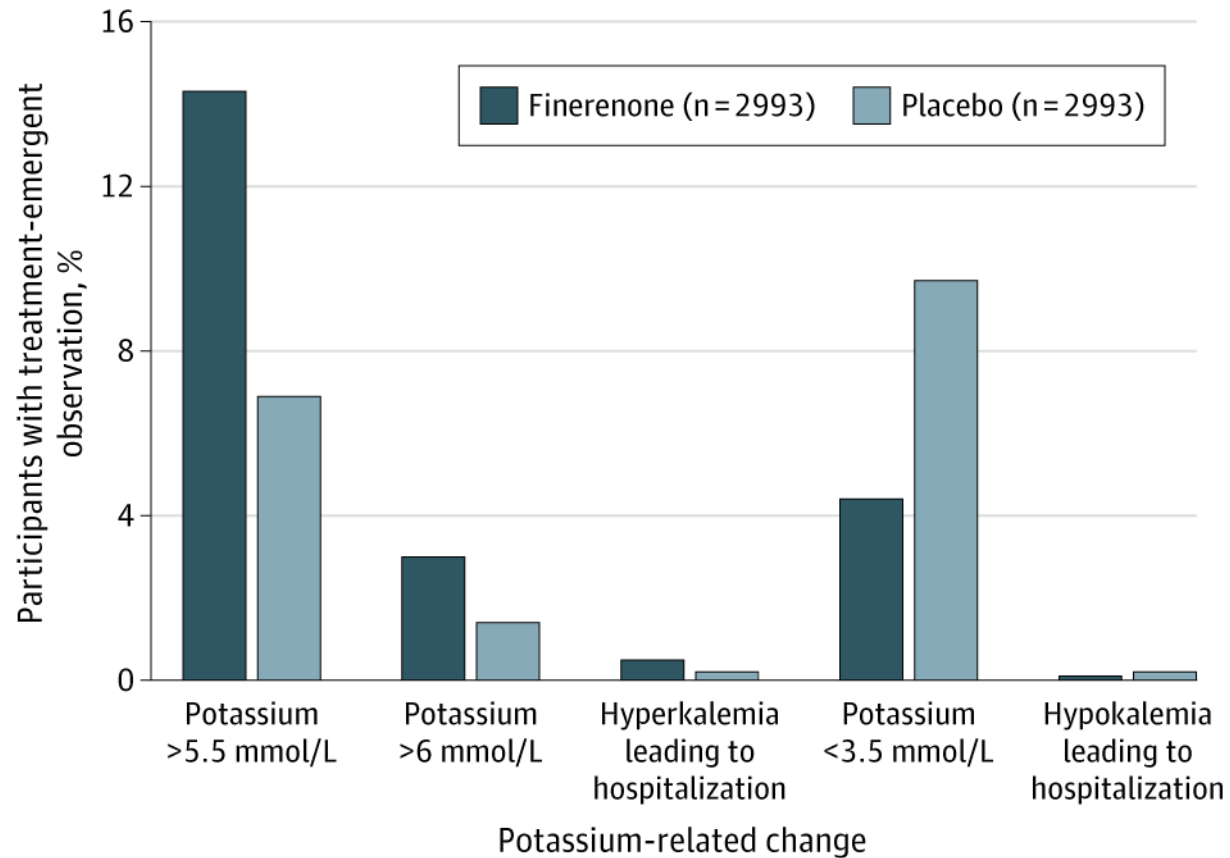


Secondary outcome: time to first occurrence of HF event or CV death



safe to initiate in any clinical care setting

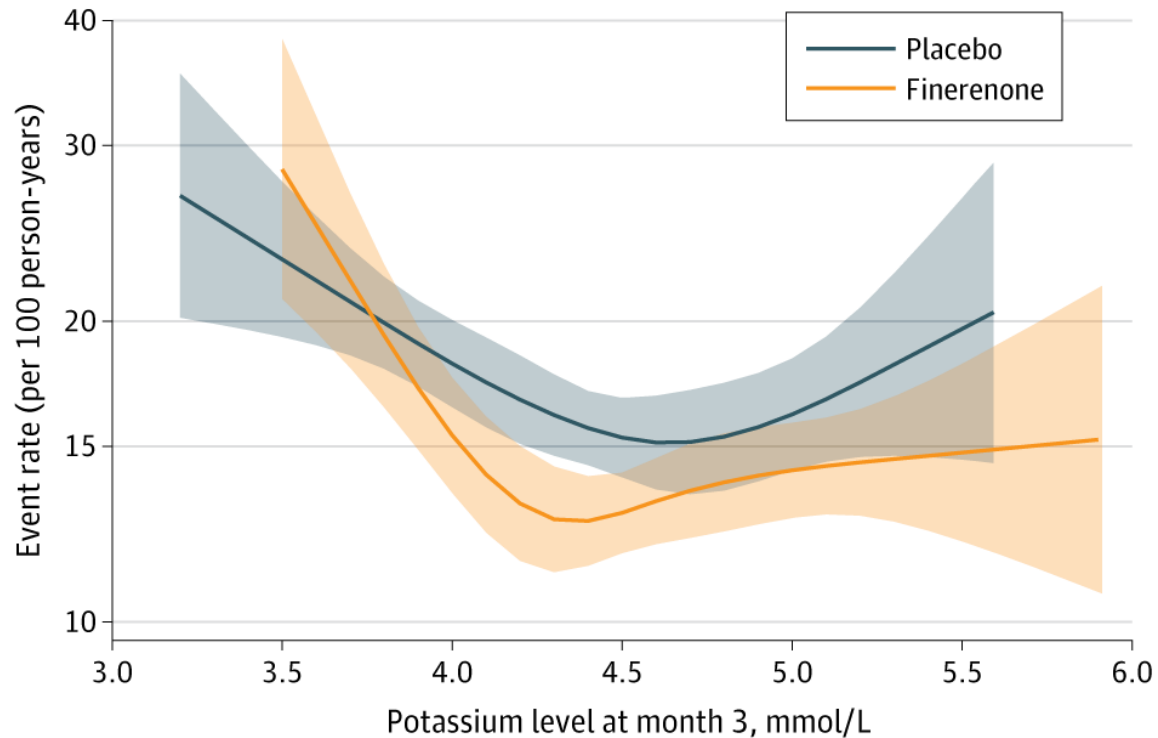
# Incidence of Investigator-Reported Potassium-Related Events in FINEARTS



In patients with HFmrEF and HFpEF, finerenone resulted in more frequent hyperkalemia and less frequent hypokalemia. No hyperkalemia or hypokalemia-related deaths were recorded in either treatment arm

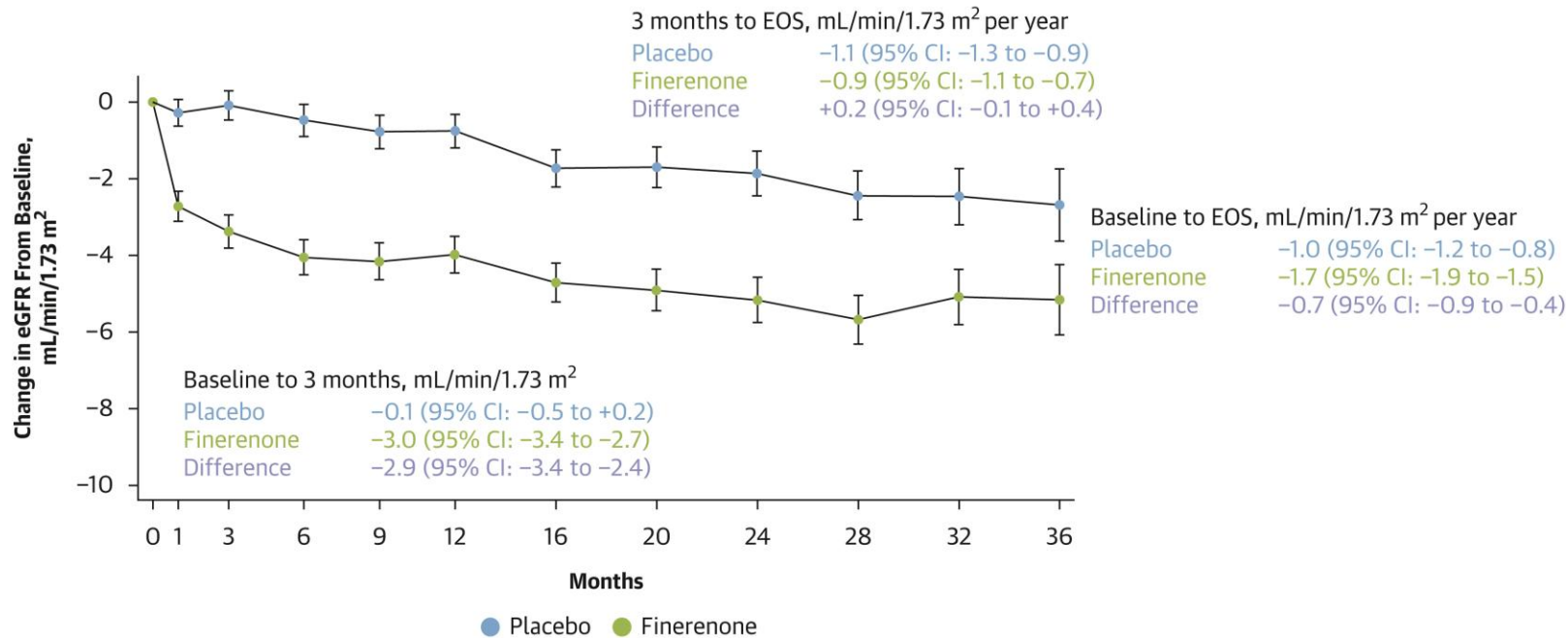
# Lower clinical risk with Finerenone even among those who develop hyperkalaemia

Incidence of CV Death or Worsening HF across serum potassium spectrum



Clinical benefit associated with finerenone relative to placebo was maintained even in those whose potassium level increased to greater than 5.5 mmol/L and <3.5 mmol/L, which are associated with a higher risk of HF events and CV death regardless of treatment arm

# Early expected hemodynamically mediated decline in GFR with Finerenone

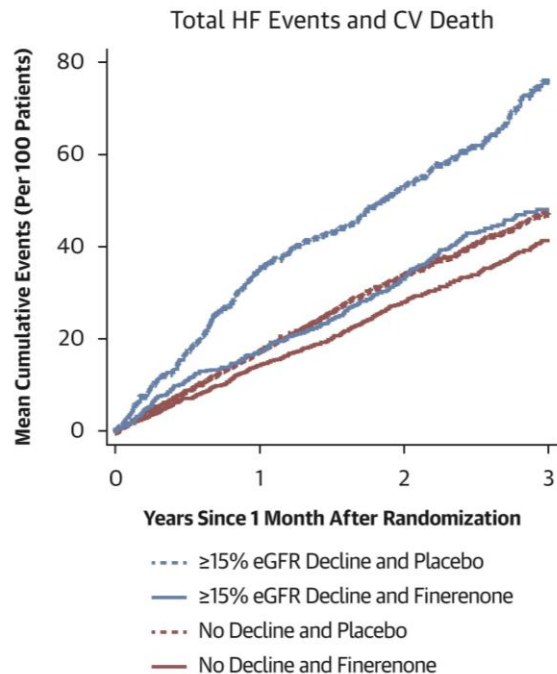


In FINEARTS-HF, a population at low risk of adverse kidney outcomes, finerenone did not significantly modify the kidney composite outcomes (sustained  $\geq 50\%$  eGFR decline or kidney failure).

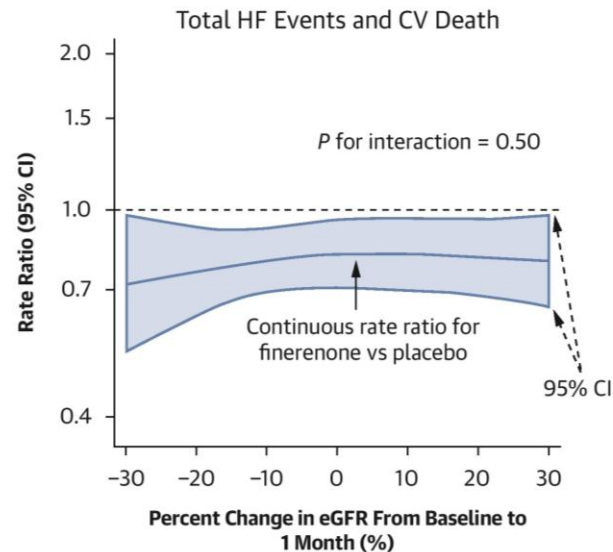
Finerenone led to a greater reduction in initial eGFR but did not result in a significant difference in chronic eGFR slope vs placebo.

# Early eGFR dip does not influence long-term treatment benefits of Finerenone

Primary Outcome According to Initial Decline in eGFR With Finerenone and Placebo



Effect of Finerenone Compared to Placebo Across Initial Percent Change in eGFR

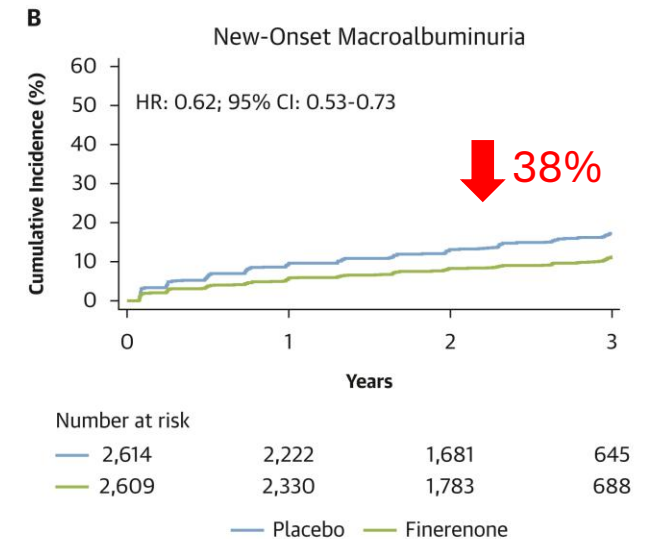
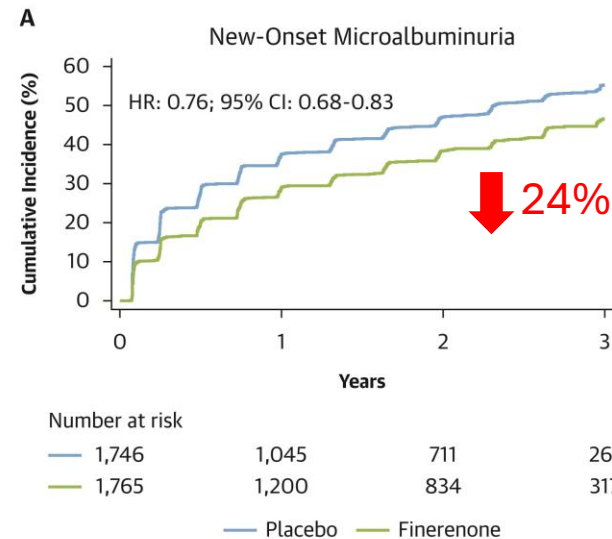
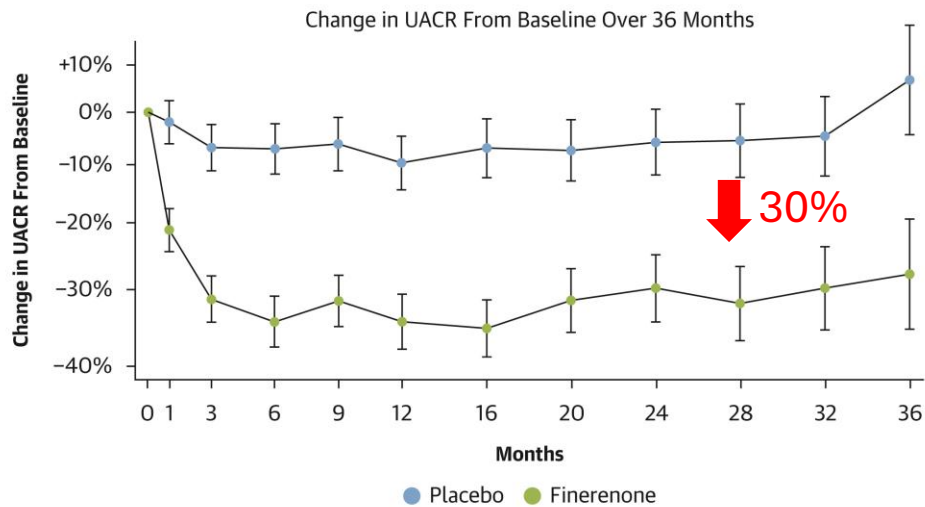


The treatment benefits of Finerenone vs. placebo were consistent regardless of the degree of eGFR decline between baseline and 1 month. An early decline in eGFR can be anticipated with finerenone and should not automatically lead to the discontinuation of this disease-modifying therapy

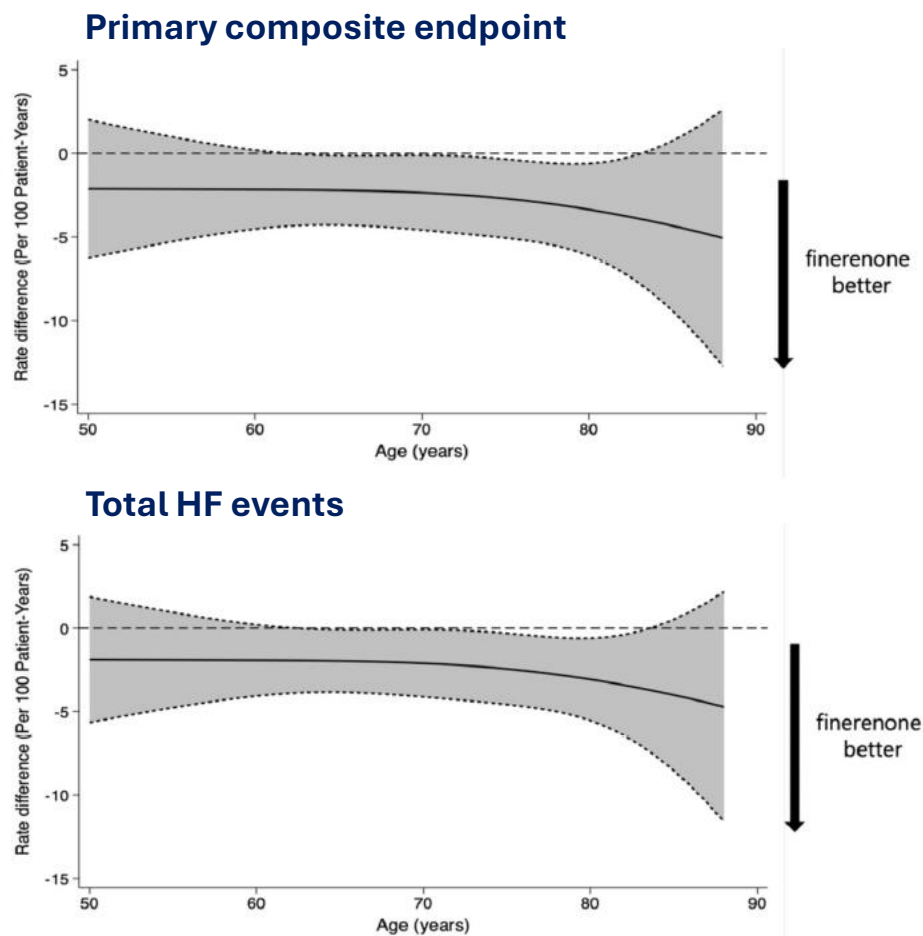
Although an initial decline in eGFR was associated with worse outcomes in patients assigned to placebo, this relationship was not as strong in those treated with finerenone.

# Early expected hemodynamically mediated decline in GFR with Finerenone

Finerenone reduced UACR by 30% (95% CI: 25%-34%) over 6 months vs placebo, an effect that persisted throughout follow-up. Finerenone reduced the risk of new-onset of microalbuminuria and macroalbuminuria by 24% (HR: 0.76; 95% CI: 0.68-0.83) and 38% (HR: 0.62; 95% CI: 0.53-0.73), respectively.



# Finerenone Improves Outcomes in Patients With HFmrEF and HFpEF Irrespective of Age: A Prespecified Analysis of FINEARTS-HF

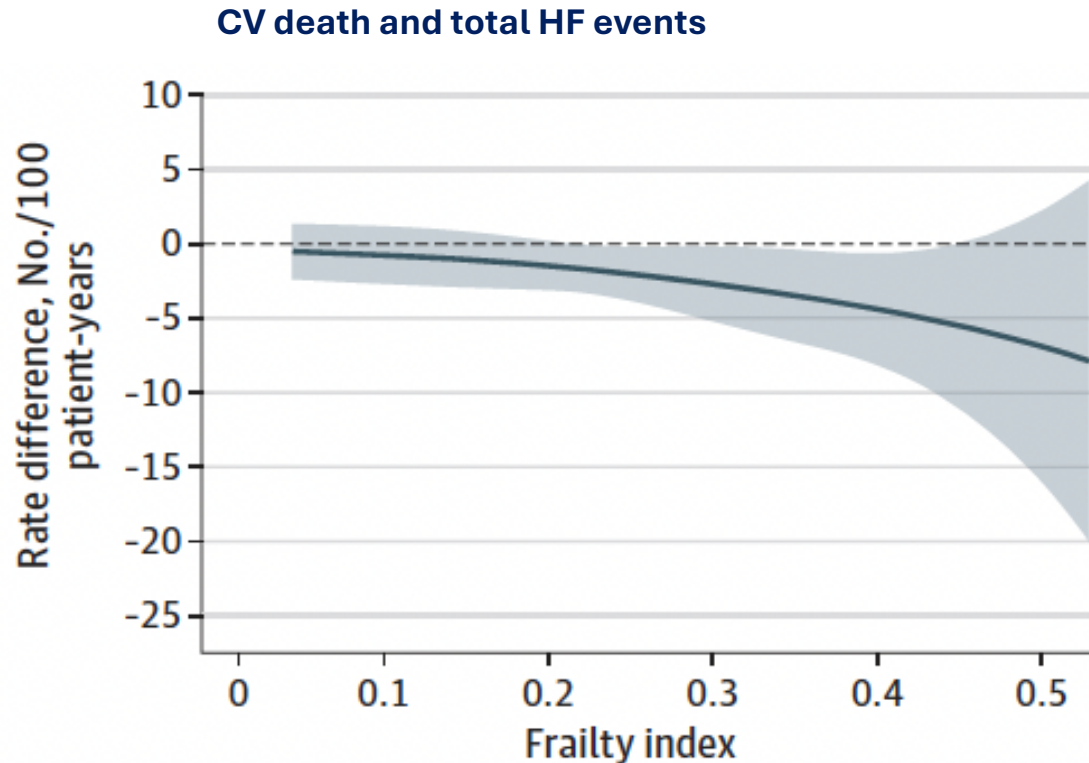


The incidence of primary outcomes increased with age. Finerenone reduced the risk of the primary outcome consistently across all age categories. Similarly, a consistent effect was observed for the components of the primary outcome.

**Finerenone reduced the risk of HF events and CV death while also improving health-related quality of life and HF symptoms in patients with HFmrEF or HFpEF across the age spectrum. Additionally, finerenone was found to be safe and well-tolerated, irrespective of age.**

# Finerenone According to Frailty in Heart Failure

## A Prespecified Analysis of the FINEARTS-HF Randomized Clinical Trial



Frailty was measured using the Rockwood cumulative deficit approach.

**In patients with HFmrEF or HFpEF, the beneficial effects of finerenone on reducing the risk of total worsening HF events and cardiovascular death and on improving symptoms were not modified by frailty status. In addition, the effects of finerenone on experiencing hypotension, elevated creatinine level, hyperkalemia, or hypokalemia did not differ by frailty status.**

# Take home messages

---

- Finerenone is a promising ns-MRA with higher selectivity than traditional MRAs. Agents such as finerenone are truly changing the way we think about mineralocorticoid receptor blockade.
- As the heart failure landscape continues to evolve, non-steroidal MRAs are increasingly recognized as a new pillar of guideline-directed medical therapy, supported by strong evidence for both renal and cardiovascular protection.
- Strong evidence from FINEARTS-HF: the trial demonstrated significant improvements in HF outcomes, particularly in patients with preserved and mildly reduced EF.
- Good safety profile: lower hyperkalaemia risk and better tolerability than steroidal MRAs.
- Effective in elderly frail patients, maintains efficacy and safety in older, vulnerable HFpEF populations.