ACOi

2022 Annual Convention & Scientific Sessions
Oct 19-22, 2022

# Update in Chronic Heart Failure:

# Bridging the Gap to GDMT

Chad Link, DO, FACC, FACOI
Cardiologist
Chairman Cardiology Department
Sparrow TCI-Lansing, MI

**Disclosures**

Speakers Bureau – Actelion Pharmaceuticals, J & &, BI, Astra Zeneca, Pfizer and BMS

# Summary

- Background of Heart Failure
- Heart Failure With Reduced LV Function (HFrEF) Guidelines Update
- Where we are at with Heart Failure with Preserved LV Function (HFpEF)and Clinical Trials from 2003-2022

# Heart Failure Terminology

- **Heart failure** is a global term for the physiological state in which cardiac output is insufficient for the body's needs. Heart Failure is a condition in which a problem with the structure or function of the heart impairs its ability to supply sufficient blood flow to meet the body's needs.

# Heart Failure Pathophysiology

**Heart failure is caused by any condition which reduces the efficiency of the myocardium leading to overload on the myocardium. Over time the increased workload will produce changes to the heart:**

- Reduced contractility, or force of contraction, due to overloading of the ventricle.
- A reduced stroke volume, as a result of a failure of systole, diastole or both.
- Increased heart rate, stimulated by increased sympathetic activity in order to maintain cardiac output.
- Hypertrophy of the myocardium, caused by the terminally differentiated heart muscle fibers increasing in size in an attempt to improve contractility.
- Enlargement of the ventricles, contributing to the enlargement and spherical shape of the failing heart.

# Heart Failure Statistics

***Prevalence***

- Heart failure (HF) affects an estimated 5.1 million Americans ≥ 20 years of age.
- 400,000 new cases of heart failure are diagnosed in the United States annually.

***Incidence***

- One-percent of adults 50 to 60 years of age.
- Ten-percent of adults 80 years of age or older.

***Mortality and Morbidity***

- At 40 years of age, the lifetime risk of developing HF for both men and women is 1 in 5; at 80 years of age, the lifetime risk of developing new HF is 20%.
- Most frequent cause of hospitalizations in the elderly and is responsible for 7 to 12 percent of all hospital admissions.

# Categorization of Heart Failure

**There are many different ways to categorize heart failure, including:**

- Which side of the heart involved (left heart failure versus right heart failure)

- Whether the abnormality is due to contraction (systolic dysfunction) or relaxation of the heart (diastolic)

- Degree of functional impairment conferred by the abnormality (as in the NYHA functional classification)

- Whether the problem is primarily increased venous back pressure (behind) the heart, or failure to supply adequate arterial perfusion (in front of) the heart (backward vs. forward failure)

- Whether the abnormality is due to low cardiac output with high systemic vascular resistance or high cardiac output with low vascular resistance (low-output heart failure vs. high-output heart failure)

# Types of Heart Failure

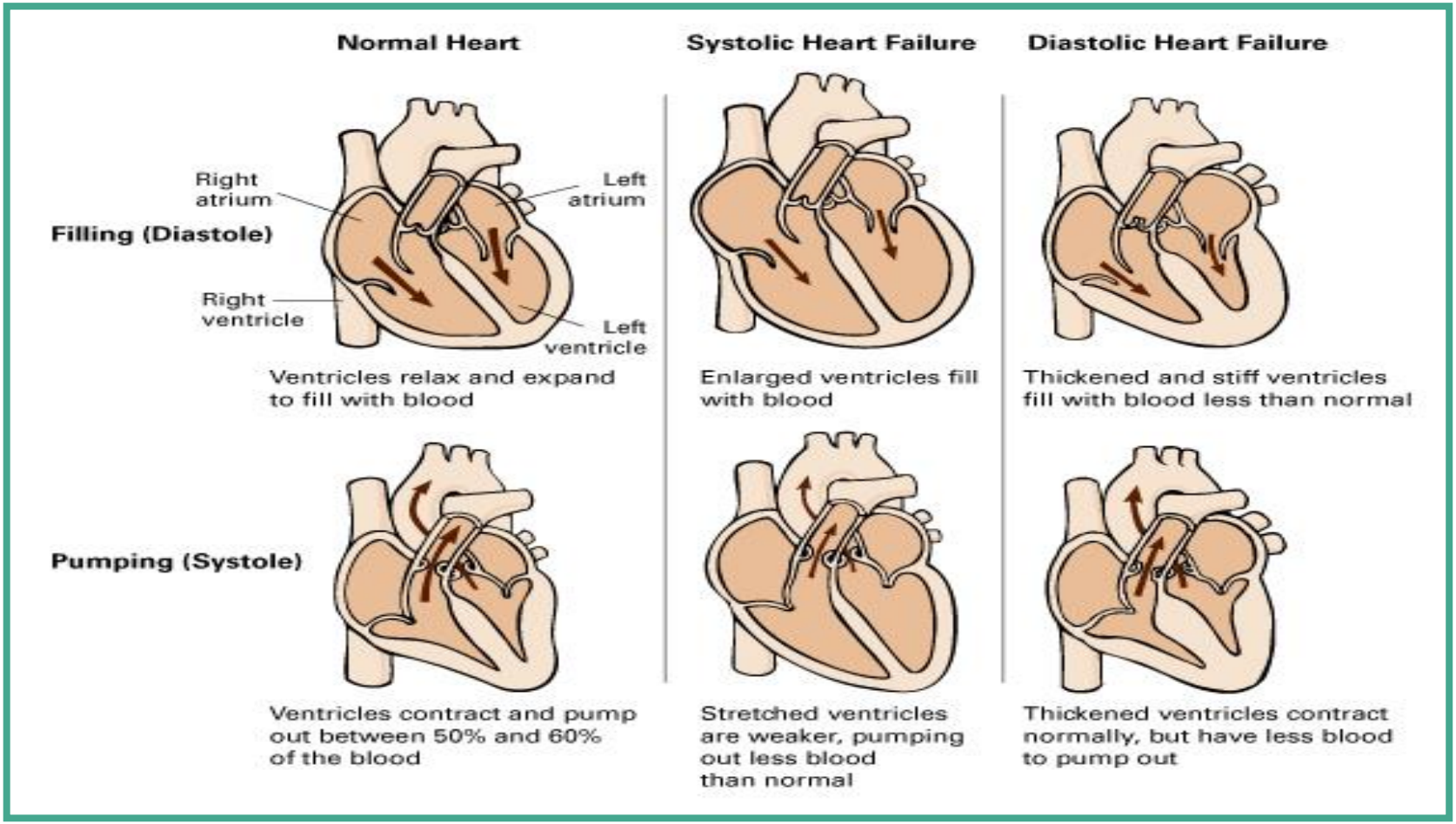
**Classification of heart failure is based on which heart function or which side of the heart is most affected by the condition.**

- ***Systolic heart failure*** ***(Correct term is HFrEF)*** – failure of contraction to pump blood out of the chambers. This is measured by ejection fraction (EF) or the percentage of blood that is ejected out of the ventricle. EF 39% or lower

- ***Diastolic heart failure*** ***(Correct term is HFpEF)*** – failure of relaxation to fill the chambers with blood- EF is 50% or greater

- ***Heart failure with mid-range EF*** ***(Correct term is HFmEF)*** – EF 40-49%

# HFrEF and HFpEF



# Characteristics of HFpEF as Compared with Those of HFrEF

**Table 1. Characteristics of Diastolic Heart Failure as Compared with Those of Systolic Heart Failure.***

| Characteristic | Diastolic Heart Failure | Systolic Heart Failure |
|---|---|---|
| Clinical features | | |
| Symptoms (e.g., dyspnea) | Yes | Yes |
| Congestive state (e.g., edema) | Yes | Yes |
| Neurohormonal activation (e.g., brain natriuretic peptide) | Yes | Yes |
| Left ventricular structure and function | | |
| Ejection fraction | Normal | Decreased |
| Left ventricular mass | Increased | Increased |
| Relative wall thickness† | Increased | Decreased |
| End diastolic volume | Normal | Increased |
| End diastolic pressure | Increased | Increased |
| Left atrial size | Increased | Increased |
| Exercise | | |
| Exercise capacity | Decreased | Decreased |
| Cardiac output augmentation | Decreased | Decreased |
| End diastolic pressure | Increased | Increased |

* The clinical features of diastolic heart failure are similar to those of systolic heart failure, but left ventricular structure and function are distinctly different.

† The descriptor of left ventricular geometry is the relative wall thickness, defined as the ratio of left ventricular wall thickness to the radius of the left ventricular cavity.

# 2021 ACC Expert Consensus

EXPERT CONSENSUS DECISION PATHWAY

## 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction

A Report of the American College of Cardiology Solution Set Oversight Committee

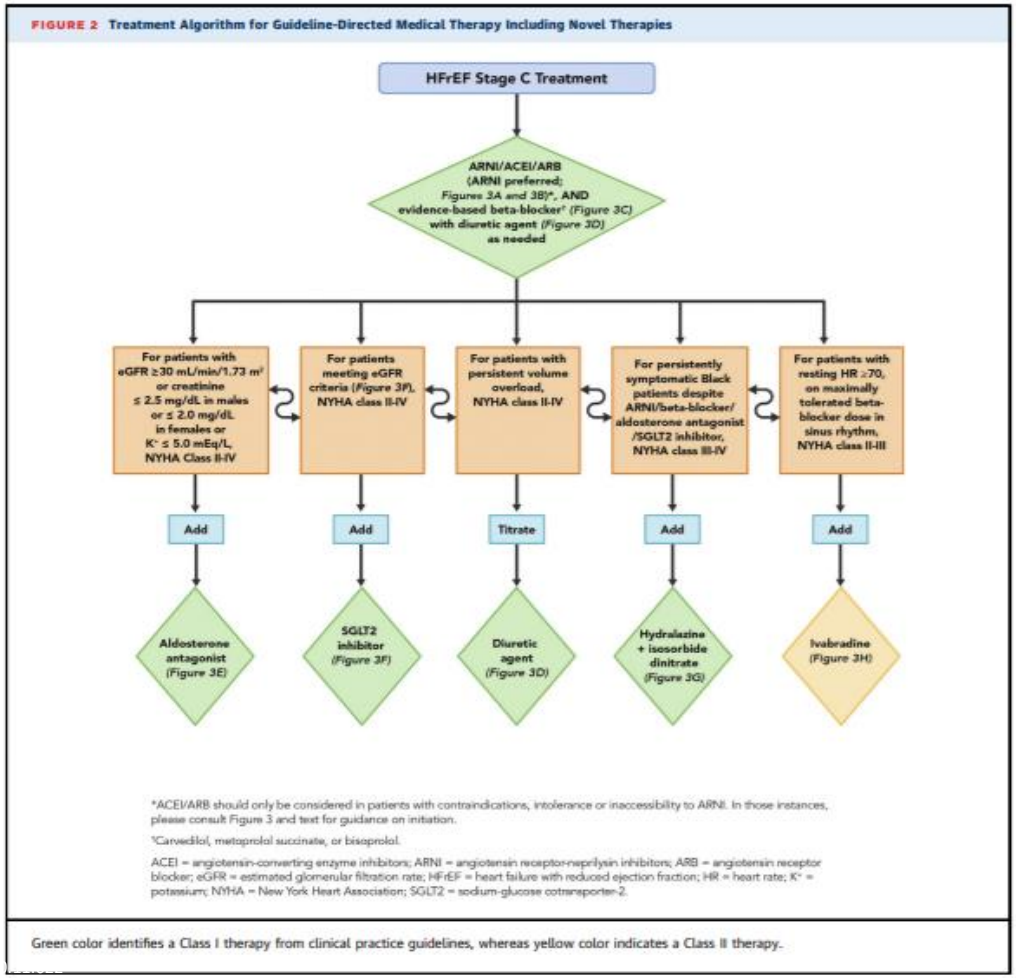

**Writing Committee**

Thomas M. Maddox, MD, MSc, FACC, *Chair*
James L. Januzzi, Jr, MD, FACC, *Vice Chair*
Larry A. Allen, MD, MHS, FACC
Khadijah Breathett, MD, MS, FACC
Javed Butler, MD, MBA, MPH, FACC
Leslie L. Davis, PhD, RN, ANP-BC, FACC
Gregg C. Fonarow, MD, FACC
Nasrien E. Ibrahim, MD, FACC
JoAnn Lindenfeld, MD, FACC
Frederick A. Masoudi, MD, MSPH, FACC
Shweta R. Motiwala, MD, MPH
Estefania Oliveros, MD, MSc
J. Herbert Patterson, PharmD
Mary Norine Walsh, MD, MACC
Alan Wasserman, MD, FACC
Clyde W. Yancy, MD, MSc, MACC
Quentin R. Youmans, MD

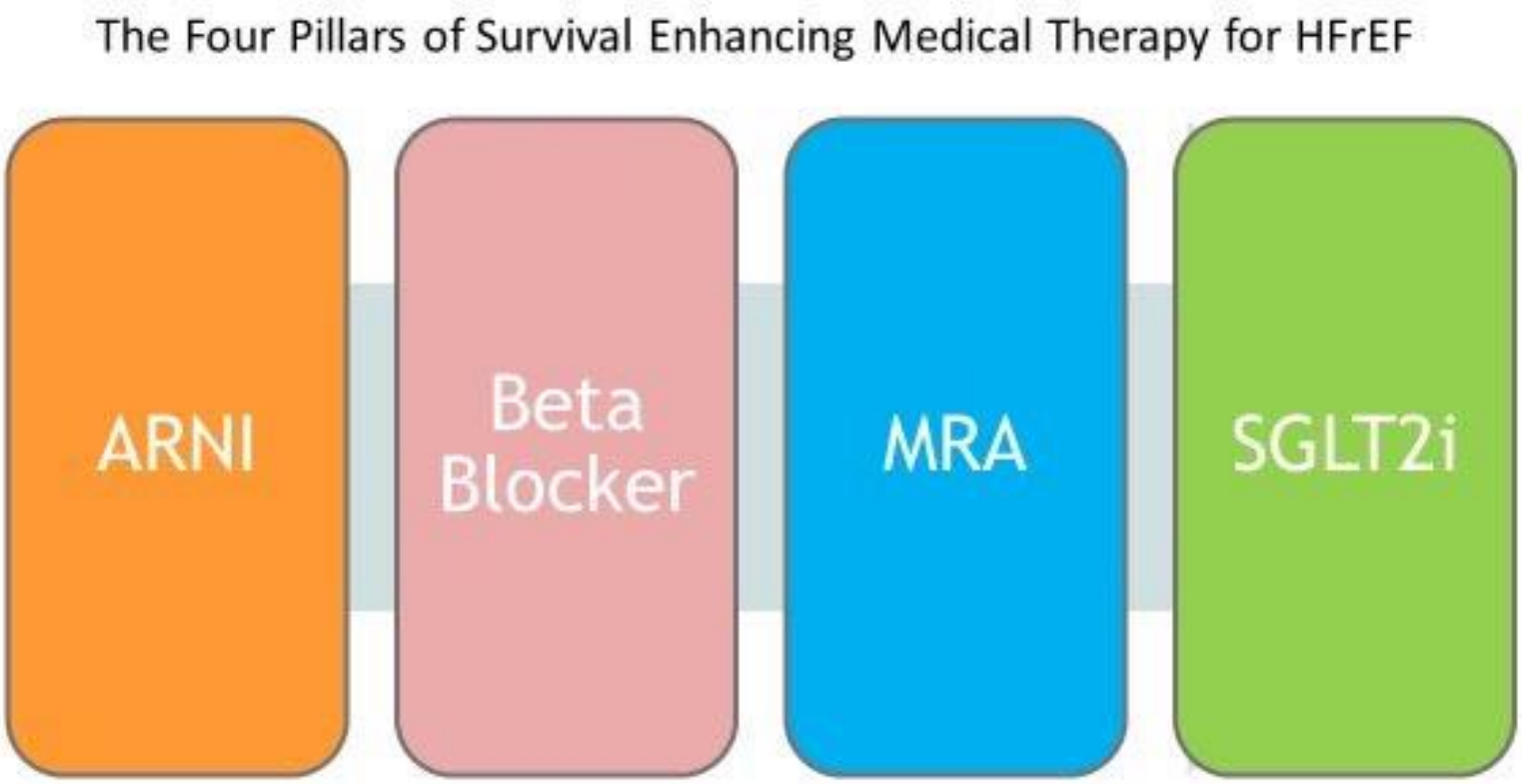
**Solution Set Oversight Committee**

Ty J. Gluckman, MD, FACC, *Chair*
Niti R. Aggarwal, MD, FACC
Nicole M. Bhave, MD, FACC
Gregory J. Dehmer, MD, MACC
Olivia N. Gilbert, MD, MSc, FACC
Chayakrit Krittanawong, MD
Dharam J. Kumbhani, MD, SM, FACC
Javier A. Sala-Mercado, MD, PhD
David E. Winchester, MD, MS, FACC
Martha Gulati, MD, MS, FACC—*Ex Officio*

# 2021 ACC Expert Consensus



# Current Recommendations for Treatment of HFrEF




Updated from Fonarow GC, et al. Am Heart J 2011;161:1024-1030 and Lancet 2008;372:1195-1196; Bassi NS et al JAMA Cardiol 2020, May 6, e200898

# Current Recommendations for Treatment of CHF

HFSA
HEART FAILURE SOCIETY OF AMERICA

JCF Journal of Cardiac Failure

## 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

Heidenreich PA, *et al. J Card Fail* 2022

# Current Recommendations for Treatment of CHF

1. GDMT for HFrEF includes 4 medication classes that include SGLT2i
2. SGLT2i have a 2a recommendation in HFmrEF
3. New recommendations for HFpEF for SGLT2i (2a), MRAs (2b) & ARNi (2b)
4. Improved LVEF refers to HFrEF where LVEF is now >40%; these patients should continue HFrEF treatment
5. Value statements for recommendations where high-quality, cost-effectiveness studies have been published
6. Amyloid heart disease has new recommendations for screening, testing and treatment
7. Evidence supporting increased filling pressures is important for HF diagnosis if LVEF >40%

2022 ACC/AHA/HFSA Guideline for the Management of Heart Failure - DOI: 10.1016/j.cardfail.2022.02.010

HFSA HEART FAILURE SOCIETY OF AMERICA

JCF Journal of Cardiac Failure

Heidenreich PA, *et al. J Card Fail* 2022

# New Recommendations for HFpEF

| COR | LOE | Recommendations |
|---|---|---|
| 2a | B - R | In patients with HFpEF, **SGLT2i** can be beneficial in decreasing HF hospitalizations and cardiovascular mortality |
| 2b | B - R | In selected patients with HFpEF, **MRAs** may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum |
| 2b | B - R | In selected patients with HFpEF, **ARNi** may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum |

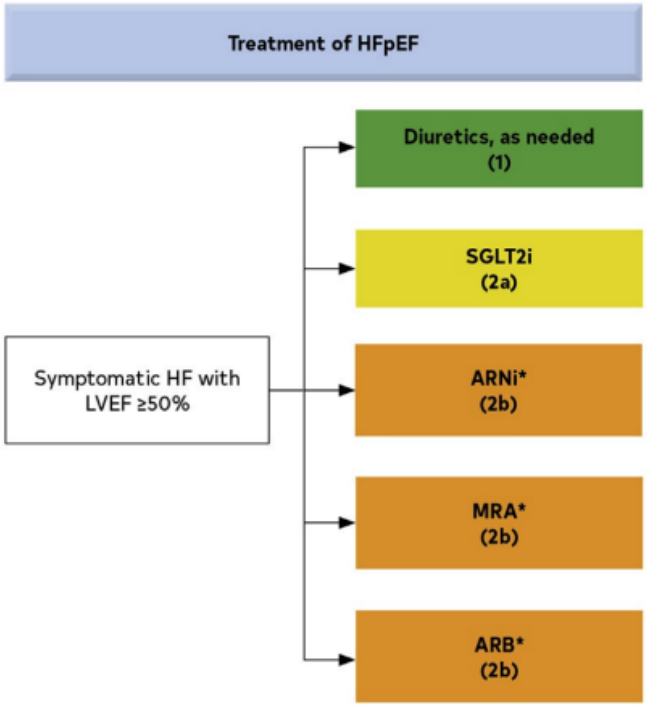
2022 ACC/AHA/HFSA Guideline for the Management of Heart Failure - DOI: 10.1016/j.cardfail.2022.02.010

HFSA HEART FAILURE SOCIETY OF AMERICA

JCF Journal of Cardiac Failure

Heidenreich PA, *et al. J Card Fail* 2022

# New Recommendations for HFpEF




2022 ACC/AHA/HFSA Guideline for the Management of Heart Failure - DOI: 10.1016/j.cardfail.2022.02.010

HFSA HEART FAILURE SOCIETY OF AMERICA

JCF Journal of Cardiac Failure

Heidenreich PA, *et al. J Card Fail* 2022

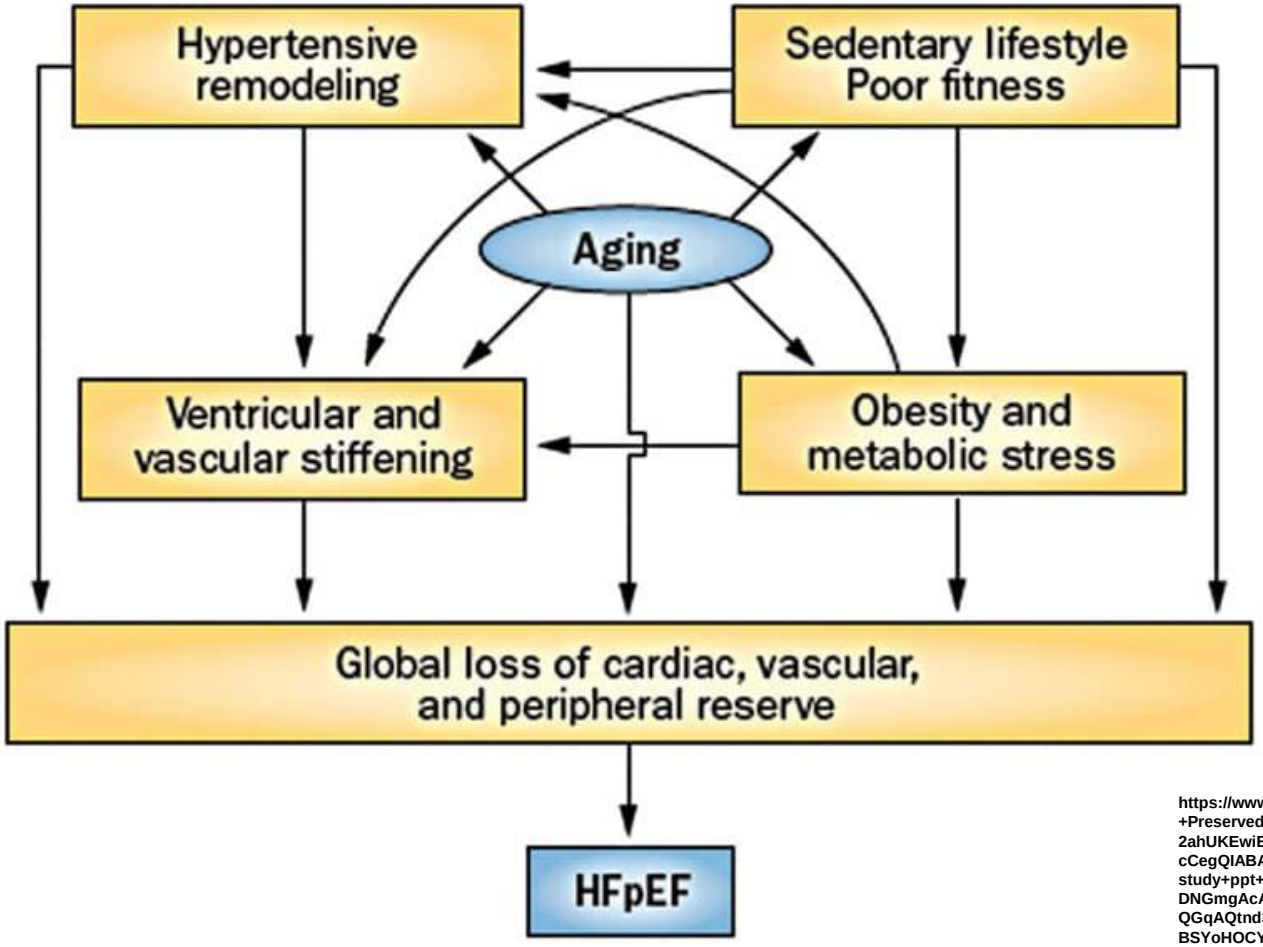
# Current Recommendations for Treatment of Patients with HFpEF

## Heart Failure with Preserved Ejection Fraction

- High rates of death and hospitalizations for HF
- High burden of debilitating symptoms and physical limitations
- No therapies with Class I recommendation in guidelines
- No therapies convincingly shown to improve health status (symptoms, physical limitations and quality of life) and exercise function

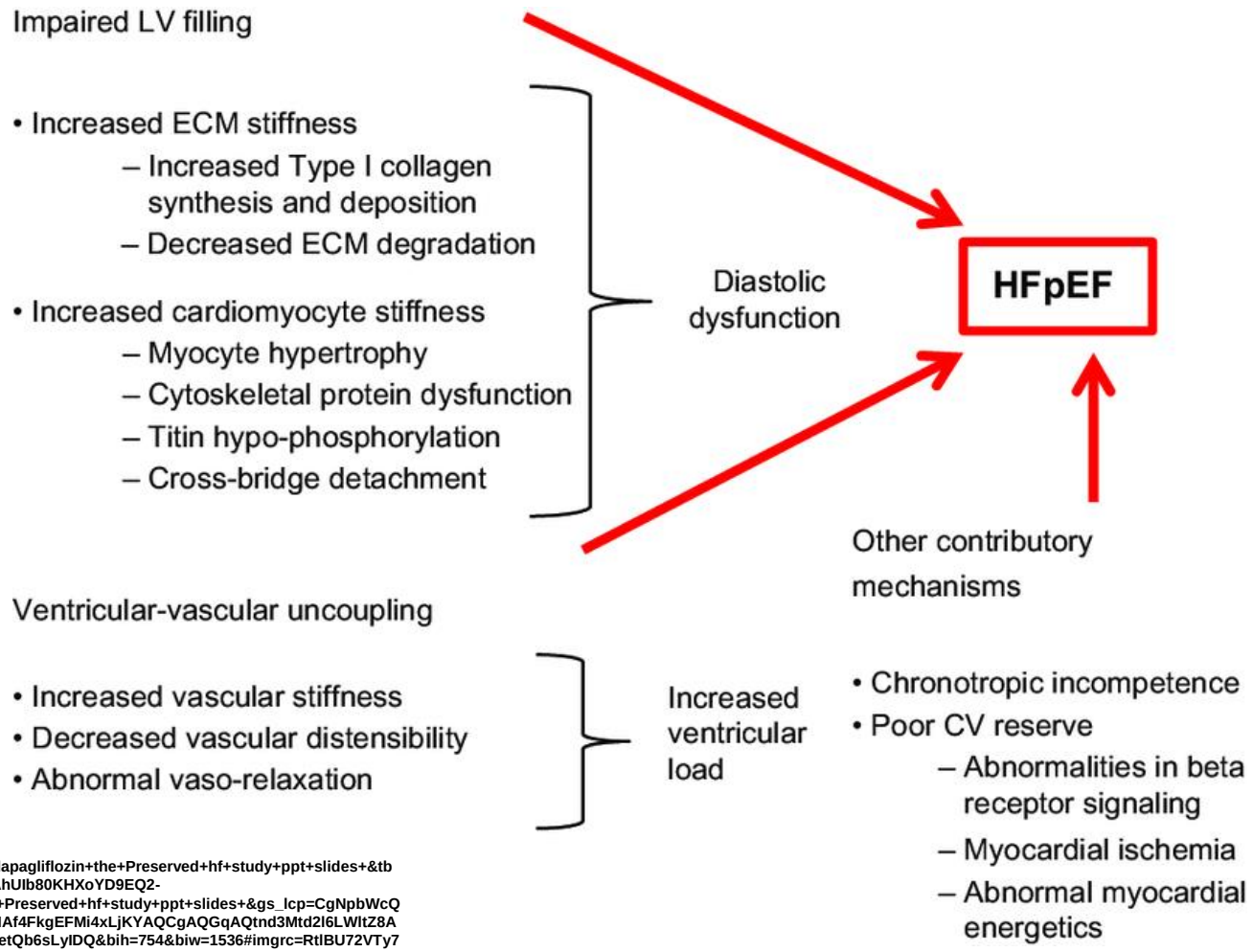
PRESERVED-HF
Effects of Dapagliflozin on Biomarkers, Symptoms and Functional Status in Patients with PRESERVED Ejection Fraction Heart Failure

# Current Recommendations for Treatment of Patients with HFpEF




https://www.google.com/search?q=dapagliflozin+the+Preserved+hf+study+ppt+slides+&tbm=isch&ved=2ahUKEwiB6_P1moj3AhUIb80KHXoYD9EQ2-cCegQIABAA&oq=dapagliflozin+the+Preserved+hf+study+ppt+slides+&gs_lcp=CgNpbWcQA1D4BljJCmDNGmgAcAB4AIABjwKIAf4FkgEFMi4xLjKYAQCgAQGqAQtnd3Mtd2l6LWltZ8ABAQ&sclient=img&ei=6iBSYoHOCYjetQb6sLylDQ&bih=754&biw=1536#imgrc=RtlBU72VTy70MM&imgdii=uOzooPAD1tZ3mM

# Current Recommendations for Treatment of Patients with HFpEF




https://www.google.com/search?q=dapagliflozin+the+Preserved+hf+study+ppt+slides+&tbm=isch&ved=2ahUKEwiB6_P1moj3AhUlb80KHXoYD9EQ2-cCegQIABAA&oq=dapagliflozin+the+Preserved+hf+study+ppt+slides+&gs_lcp=CgNpbWcQA1D4BljJCmDNGmgAcAB4AIABjwKIAf4FkgEFMi4xLjKYAQCgAQGqAQtnd3Mtd2I6LWItZ8ABAQ&sclient=img&ei=6iBSYoHOCYjetQb6sLylDQ&bih=754&biw=1536#imgrc=RtlBU72VTy70MM&imgdii=uOzooPAD1tZ3mM

# Current Recommendations for Treatment of Patients with HFpEF

## GENERAL MANAGEMENT

**Goals of therapy** — For patients with HFpEF, the goals of treatment are to reduce HF symptoms, increase functional status, and reduce the risk of hospital admission. There is no clear evidence that pharmacologic therapy, diet, or other therapies reduce the risk of mortality in patients with HFpEF.

**Ongoing evaluation and monitoring**
Chronic disease management
Exercise, diet, weight loss, and cardiac rehabilitation
Asymptomatic diastolic dysfunction

# Current Recommendations for Treatment of Patients with HFpEF

**MANAGEMENT OF ASSOCIATED CONDITIONS**

Hypertension
Atrial Fibrillation
DM
Chronic Kidney Disease
Myocardial Ischemia
Hyperlipidemia

# Current Recommendations for Treatment of Patients with HFpEF

## The dawn of a new era of targeted therapies for heart failure with preserved ejection fraction (HFpEF)

•Kenji Harada & Kazuomi Kario *Hypertension Research* **volume 45**, pages164–166 (2022)

Although effective treatments exist for heart failure with a reduced ejection fraction (HFrEF), there is a paucity of treatments with proven benefits for heart failure with a preserved ejection fraction (HFpEF). Detailed results from the phase III EMPEROR-Preserved trial were published in *The New England Journal of Medicine* on August 27, 2021 [1]. The EMPEROR-Preserved trial was a large, international, double-blind and placebo-controlled trial of empagliflozin, a sodium-glucose cotransporter 2 inhibitor (SGLT2-i), in patients with HFpEF (ejection fraction [EF] > 40%). In the trial's HFpEF patients, the SGLT2-i empagliflozin led to a 21% lower relative risk (hazard ratio [HR] 0.79, 95% confidence interval [CI]: 0.69–0.90) of the composite of cardiovascular death or hospitalization for heart failure, which was related mainly to a 29% lower risk (HR 0.73, 95% CI: 0.61–0.88) of heart failure hospitalization associated with empagliflozin treatment.

# Sodium–glucose co-transporter 2 (SGLT2) inhibitors

Sodium–glucose co-transporter 2 (SGLT2) inhibitors, originally developed as glucose-lowering agents, have been shown to reduce heart failure hospitalizations in patients with type 2 diabetes, including those without established heart failure. Moreover, in patients with heart failure and reduced left ventricular ejection fraction (LVEF ≤40%; HFrEF), including those with and without type 2 diabetes, both dapagliflozin and empagliflozin reduced cardiovascular death or heart failure events when added to standard therapy.

https://onlinelibrary.wiley.com/doi/10.1002/ejhf.2249

# Sodium–glucose co-transporter 2 (SGLT2) inhibitors

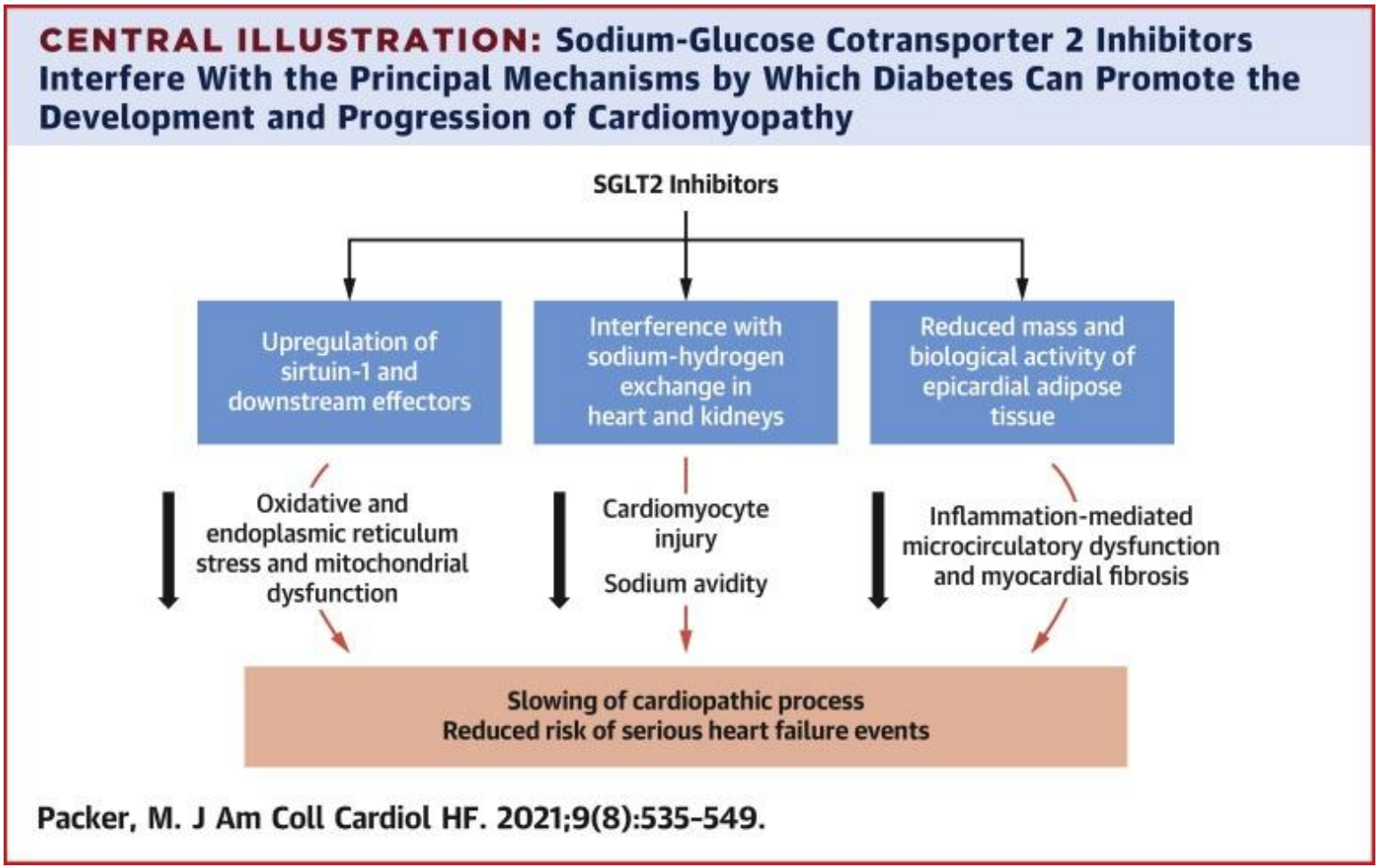
While the mechanisms by which SGLT2 inhibitors improve outcomes in heart failure continue to be investigated, they are postulated to include favorable effects on haemodynamics,[6, 7] improvement in myocardial energetics and loading conditions, favorable effects on endothelial function and inflammation, and slowing of the progression of kidney disease.[8] These effects may collectively underlie observed early and sustained improvements in filling pressures and ventricular remodeling.[7, 9-11]

Patients with preserved or mildly reduced ejection fraction (LVEF >40%) now represent the majority of those with heart failure, and experience a comparable burden of poor outcomes, such as death, hospitalizations and symptom burden, as those with LVEF ≤40%; yet suffer from dearth of effective therapies.

Therefore, there is a large and urgent unmet clinical need for efficacious and safe treatments in this vulnerable patient group.

https://onlinelibrary.wiley.com/doi/10.1002/ejhf.2249

# Sodium–glucose co-transporter 2 (SGLT2) inhibitors



# Current Recommendations for Treatment of Patients with HFpEF

**CHARM PRESERVED (2003)**

**TOPCAT (2013)**

**PARAGON-HF (2019)**

**EMPEROR PRESERVED (2021)**

**PRESERVED-HF (2021)**

**SOLOIST-HF/ SCORED (2021)**

**DELIVER (2022)**

**VITALITY-HFpEF (2022)**

**FINEARTS-HF (2024)**

# CHARM PRESERVED (2003)

## CHARM-Preserved: Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity - Preserved

**Purpose**

To determine whether the angiotensin II receptor blocker candesartan is beneficial in patients with chronic heart failure (CHF) and preserved left ventricular systolic function

**Reference**

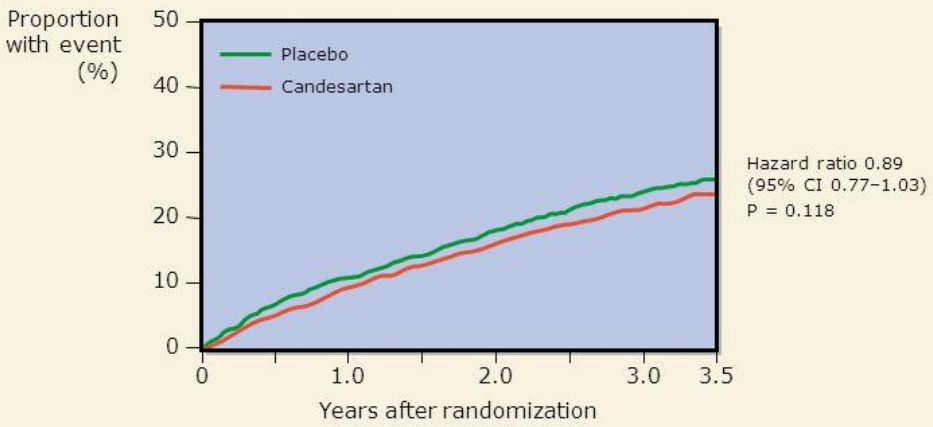
**Yusuf S, Pfeffer MA, Swedberg K, et al. for the CHARM Investigators and Committees.** Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: the CHARM-Preserved trial. *Lancet* 2003;**362**:777–81.

charm preserved clinical trial ppt - Google Search

# CHARM PRESERVED (2003)

## CHARM-Preserved:
## Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity - Preserved
## *- RESULTS continued -*

**Cardiovascular death or hospital admission for CHF**




Yusuf et al. *Lancet* 2003;**362**:777–81.

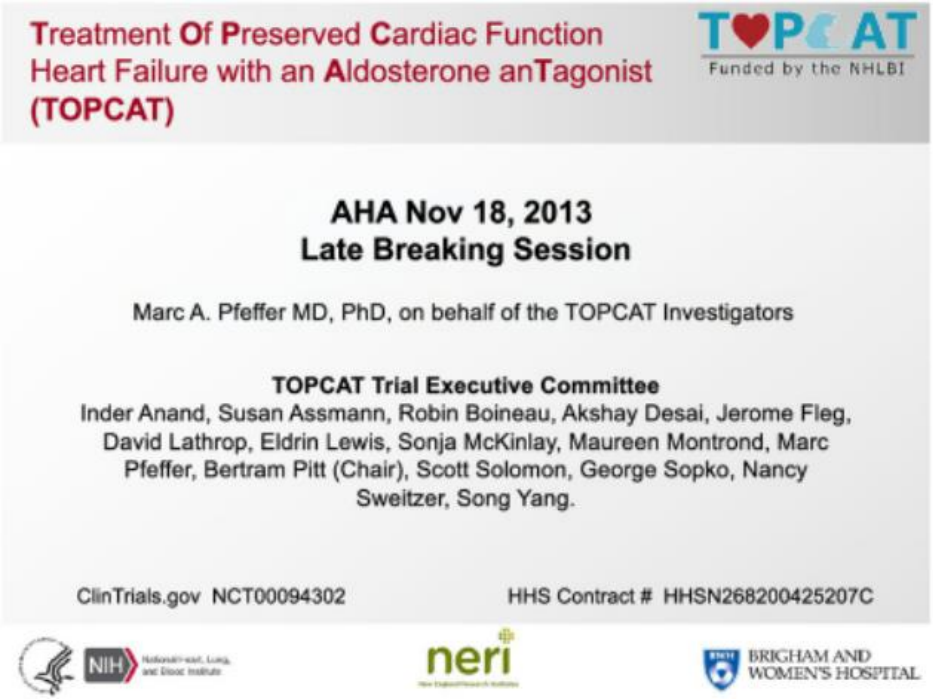
charm preserved clinical trial ppt - Google Search

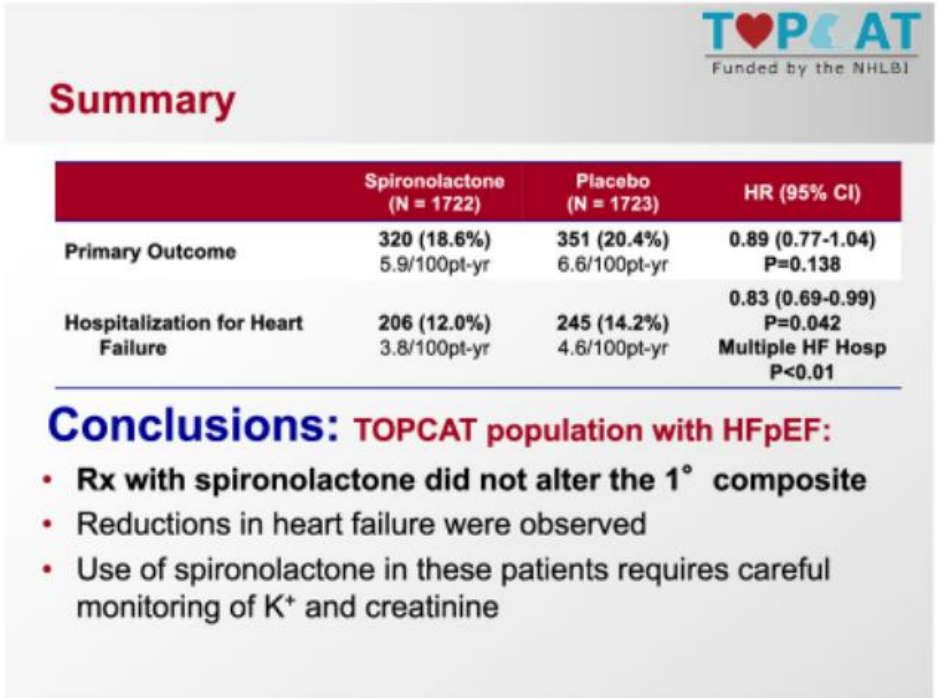
# TOPCAT (2013)

**MRA** – In trials that included patients with HFpEF, MRAs reduced the risk of HF hospitalization but did not clearly reduce the risk of mortality. The benefit of MRA therapy must be weighed against the risk of hyperkalemia.

Evidence to support this approach comes from the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trial and from subgroup analyses that studied regional differences in trial procedures

# TOPCAT (2013)




https://evidence.nejm.org/doi/full/10.1056/EVIDctcs2100007

# TOPCAT (2013)

The TOPCAT trial randomly assigned 3445 patients with symptomatic HF and LVEF ≥45 percent (median 56 percent) to receive either spironolactone or placebo. The composite primary outcome (death from cardiovascular causes, aborted cardiac arrest, or hospitalization for HF) was lower but not statistically different with spironolactone compared with placebo (18.6 and 20.4 percent, respectively; HR 0.89, 95% CI 0.77-1.04). Hospitalization for HF was less frequent in the spironolactone group (12.0 percent) compared with the placebo group (14.2 percent; HR 0.83, 95% CI 0.69-0.99), but other components of the primary outcome occurred at similar rates in the two treatment groups. Total deaths and total hospitalizations were similar in the spironolactone and placebo groups.)

# TOPCAT (2013)

When compared with the control group, the spironolactone group had a higher rate of hyperkalemia (19 versus 9 percent) and a higher rate of increased creatinine levels (10 versus 7 percent).

# TOPCAT (2013)

NEJM Evidence

CURRENT ISSUE RECENTLY PUBLISHED AUTHOR CENTER ABOUT

CLINICAL TRIALS CASE STUDY

## Behind the Scenes of TOPCAT — Bending to Inform

Marc A. Pfeffer, M.D., Ph.D.[1] and Brian Claggett, Ph.D.[1]

Show More

Tweet

Published January 10, 2022
NEJM Evid 2022; 1 (1)
DOI: https://doi.org/10.1056/EVIDctcs2100007

Issue ›

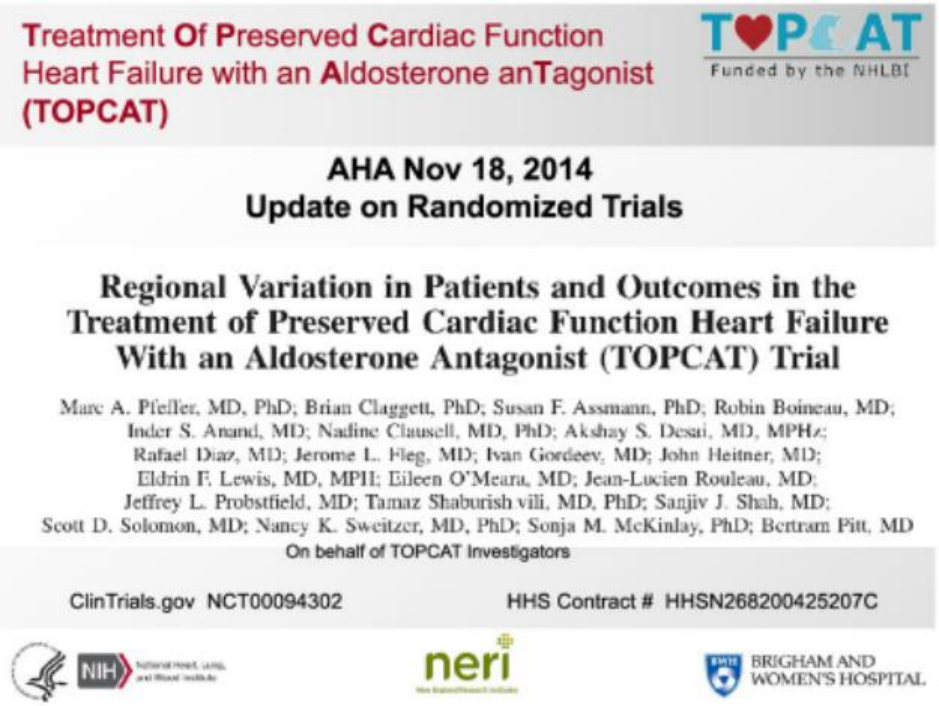
https://evidence.nejm.org/doi/full/10.1056/EVIDctcs2100007

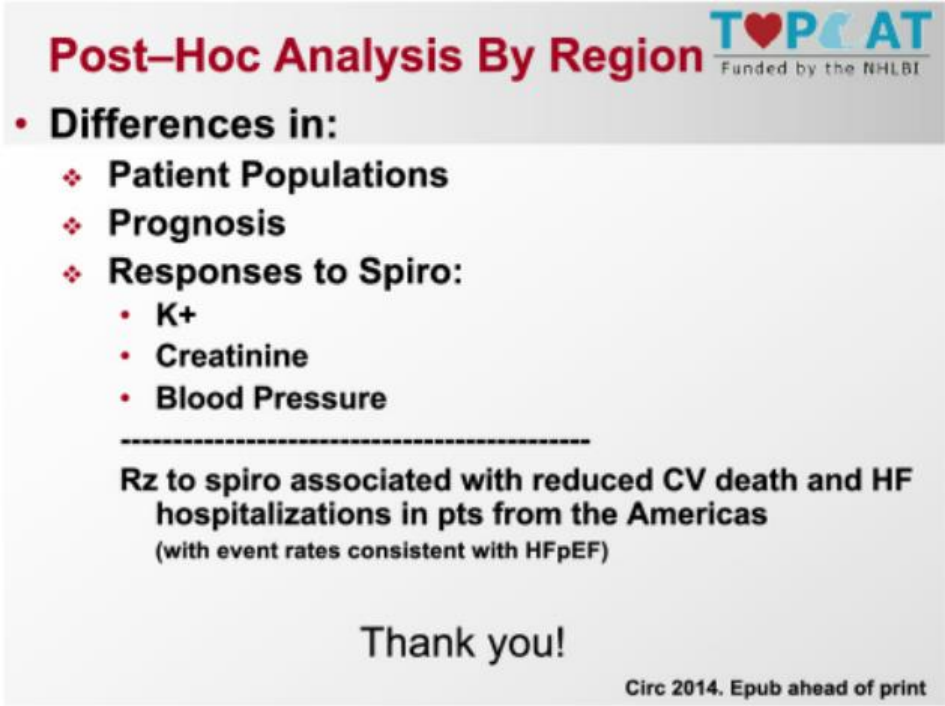
# TOPCAT (2014)

In subgroup analyses focused on regional effects, the efficacy of spironolactone was greater in the Americas (primary outcome 27 versus 32 percent with placebo) when compared with Russia/Georgia (9 versus 8 percent with placebo). In addition, compliance was higher in the Americas when compared with Russia/Georgia.

These differences suggest poorer adherence to the trial procedures outside of the Americas and raise questions about the veracity of the HFpEF diagnosis in this cohort as well. In a post hoc analysis of the trial that excluded Russia/Georgia, spironolactone reduced the risk of the primary outcome (27.3 versus 31.8 percent; HR 0.82, 95% CI 0.69-0.98).

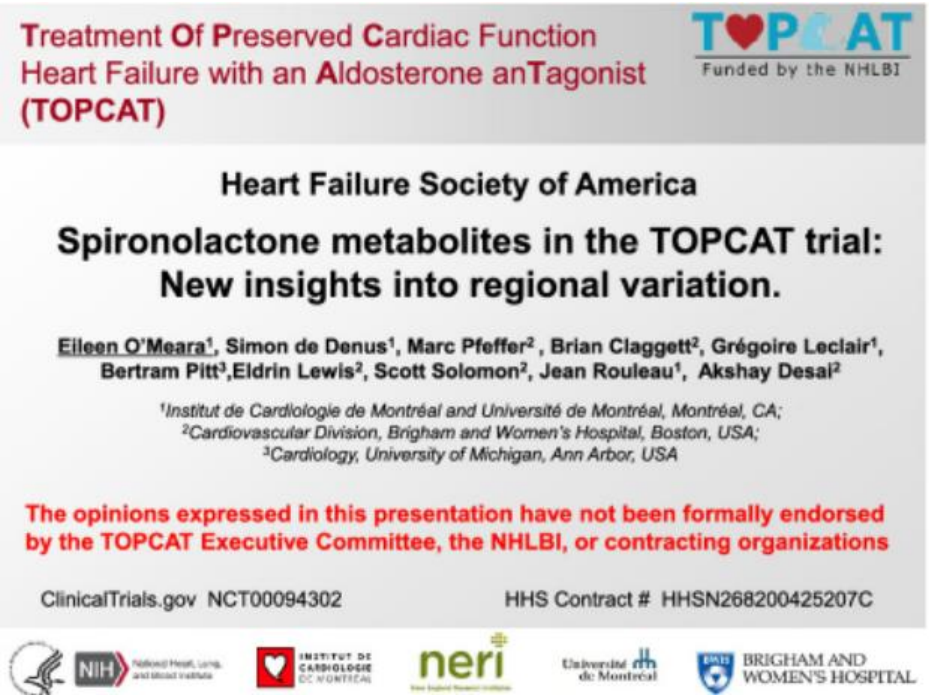
# TOPCAT (2014)




https://evidence.nejm.org/doi/full/10.1056/EVIDctcs2100007

# TOPCAT (2014)



Treatment Of Preserved Cardiac Function Heart Failure with an Aldosterone anTagonist (TOPCAT)

TOPCAT Funded by the NHLBI

Heart Failure Society of America

## Spironolactone metabolites in the TOPCAT trial: New insights into regional variation.

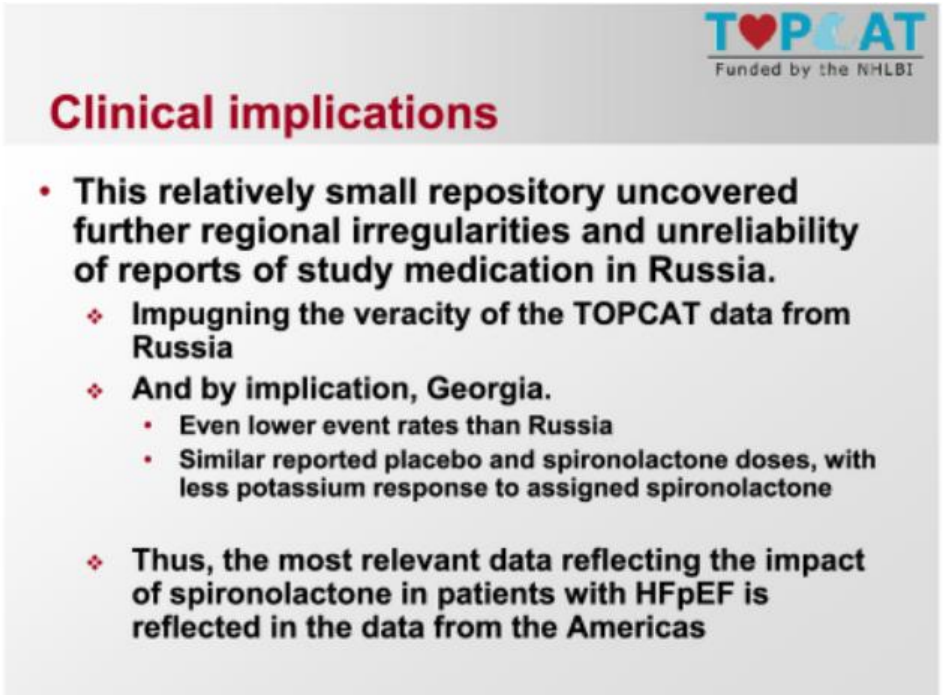
Eileen O'Meara[1], Simon de Denus[1], Marc Pfeffer[2], Brian Claggett[2], Grégoire Leclair[1], Bertram Pitt[3], Eldrin Lewis[2], Scott Solomon[2], Jean Rouleau[1], Akshay Desai[2]

[1]Institut de Cardiologie de Montréal and Université de Montréal, Montréal, CA; [2]Cardiovascular Division, Brigham and Women's Hospital, Boston, USA; [3]Cardiology, University of Michigan, Ann Arbor, USA

The opinions expressed in this presentation have not been formally endorsed by the TOPCAT Executive Committee, the NHLBI, or contracting organizations

ClinicalTrials.gov NCT00094302 HHS Contract # HHSN268200425207C

NIH · Institut de Cardiologie de Montréal · neri · Université de Montréal · Brigham and Women's Hospital



TOPCAT Funded by the NHLBI

## Clinical implications

- This relatively small repository uncovered further regional irregularities and unreliability of reports of study medication in Russia.
  - Impugning the veracity of the TOPCAT data from Russia
  - And by implication, Georgia.
    - Even lower event rates than Russia
    - Similar reported placebo and spironolactone doses, with less potassium response to assigned spironolactone
  - Thus, the most relevant data reflecting the impact of spironolactone in patients with HFpEF is reflected in the data from the Americas

https://evidence.nejm.org/doi/full/10.1056/EVIDctcs2100007

# PARAGON-HF (2019)

Angiotensin-Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction

## Hypothesis

Patient's with HFpEF will have a reduction in cardiovascular (CV) mortality and heart failure (HF) hospitalizations (first and recurrent) when taking an ARNI vs valsartan.

https://www.google.com/search?q=heart+failure+with+preserved+function+ppt&source=hp&ei=LhVSYtWPJcLRtAbCn56ACA&iflsig=AHkkrS4AAAAAYIIjPnL-L5qOOrD2Sus5kXShr5uZuN3t&ved=0ahUKEwjV3tndj4j3AhXCKM0KHcKPB4AQ4dUDCAk&uact=5&oq=heart+failure+with+preserved+function+ppt&gs_lcp=Cgdnd3Mtd2l6EAMyCAghEBYQHRAeMggIIRAWEB0QHjoUCAAQ6gIQtAIQigMQtwMQ1AMQ5QI6BAgAEEM6EQguEIAEELEDEIMBEMcBEKMCOgcILhDUAhBDOgsILhCABBDHARCjAjoICAAQgAQQsQM6CAguELEDEIMBOg4ILhCABBCxAxDHARCjAjoLCC4QgAQQsQMQgwE6BwgAELEDEEM6BQgAEIAEOgUIABCRAjoGCAAQFhAeOggIABAWEAoQHjoFCAAQhgNQ_QxY4klgnFJoAXAAeACAAWaIAZcWkgEENDAuMZgBAKABAbABCg&sclient=gws-wiz

# PARAGON-HF (2019)

| Primary outcome | Primary outcome results (rate ratio) |
|---|---|
| Composite cardiovascular (CV) mortality and hospitalization secondary to (HF) | Sacubitril-valsartan vs Valsartan:<br>0.87; 95% CI, 0.75 to 1.01<br><br>**p=0.06** |

https://www.google.com/search?q=heart+failure+with+preserved+function+ppt&source=hp&ei=LhVSYtWPJcLRtAbCn56ACA&iflsig=AHkkrS4AAAAAYIIjPnL-L5qOOrD2Sus5kXShr5uZuN3t&ved=0ahUKEwjV3tndj4j3AhXCKM0KHcKPB4AQ4dUDCAk&uact=5&oq=heart+failure+with+preserved+function+ppt&gs_lcp=Cgdnd3Mtd2l6EAMyCAghEBYQHRAeMggIIRAWEB0QHjoUCAAQ6gIQtAIQigMQtwMQ1AMQ5QI6BAgAEEM6EQguEIAEELEDEIMBEMcBEKMCOgcILhDUAhBDOgsILhCABBDHARCjAjoICAAQgAQQsQM6CAguELEDEIMBOg4ILhCABBCxAxDHARCjAjoLCC4QgAQQsQMQgwE6BwgAELEDEEM6BQgAEIAEOgUIABCRAjoGCAAQFhAeOggIABAWEAoQHjoFCAAQhgNQ_QxY4klgnFJoAXAAeACAAWaIAZcWkgEENDAuMZgBAKABAbABCg&sclient=gws-wiz

# PARAGON-HF (2019)

## Secondary outcomes & results (95% CI)

*Change in NYHA class from baseline to 8 months: **OR, 1.45 (1.13-1.86)**

All-cause mortality: HR, 0.97 (0.84-1.13)

Change in KCCQ at 8 months: Difference, 1.0 (0.0-2.1)

*Renal composite outcome: **HR, 0.50 (0.33-0.77)**

*sacubitril-valsartan had significantly more patients with improved NYHA class, and less unchanged or worsened NYHA change from baseline sacubitril-valsartan had significantly less death from renal failure, ESRD, decrease in GFR < 50% from baseline

https://www.google.com/search?q=heart+failure+with+preserved+function+ppt&source=hp&ei=LhVSYtWPJcLRtAbCn56ACA&iflsig=AHkkrS4AAAAAYIIjPnL-L5qOOrD2Sus5kXShr5uZuN3t&ved=0ahUKEwjV3tndj4j3AhXCKM0KHcKPB4AQ4dUDCAk&uact=5&oq=heart+failure+with+preserved+function+ppt&gs_lcp=Cgdnd3Mtd2l6EAMyCAghEBYQHRAeMggIIRAWEB0QHjoUCAAQ6gIQtAIQigMQtwMQ1AMQ5QI6BAgAEEM6EQguEIAEELEDEIMBEMcBEKMCOgcILhDUAhBDOgsILhCABBDHARCjAjoICAAQgAQQsQM6CAguELEDEIMBOg4ILhCABBCxAxDHARCjAjoLCC4QgAQQsQMQgwE6BwgAELEDEEM6BQgAEIAEOgUIABCRAjoGCAAQFhAeOggIABAWEAoQHjoFCAAQhgNQ_QxY4klgnFJoAXAAeACAAWaIAZcWkgEENDAuMZgBAKABAbABCg&sclient=gws-wiz

# PARAGON-HF (2019)

| Safety outcomes (p-value) | Study conclusion |
|---|---|
| *Hypotension (SBP < 100 mg Hg): **<0.001**<br><br>Elevated serum creatinine: 0.38<br><br>*Elevated serum postassium: **0.04**<br><br>*Angioedema: **0.02**<br><br>Liver-related adverse event: 0.11 | Patients with HFpEF treated with sacubitril-valsartan do not have significantly reduced risk in CV morbidity and mortality or heart failure hospitalizations (first and recurrent) to those patients taking valsartan. |

https://www.google.com/search?q=heart+failure+with+preserved+function+ppt&source=hp&ei=LhVSYtWPJcLRtAbCn56ACA&iflsig=AHkkrS4AAAAAYIljPnL-L5qOOrD2Sus5kXShr5uZuN3t&ved=0ahUKEwjV3tndj4j3AhXCKM0KHcKPB4AQ4dUDCAk&uact=5&oq=heart+failure+with+preserved+function+ppt&gs_lcp=Cgdnd3Mtd2l6EAMyCAghEBYQHRAeMggIIRAWEB0QHjoUCAAQ6gIQtAIQigMQtwMQ1AMQ5QI6BAgAEEM6EQguEIAEELEDEIMBEMcBEKMCOgcILhDUAhBDOgsILhCABBDHARCjAjoICAAQgAQQsQM6CAguELEDEIMBOg4ILhCABBCxAxDHARCjAjoLCC4QgAQQsQMQgwE6BwgAELEDEEM6BQgAEIAEOgUIABCRAjoGCAAQFhAeOggIABAWEAoQHjoFCAAQhgNQ_QxY4klgnFJoAXAAeACAAWaIAZcWkgEENDAuMZgBAKABAbABCg&sclient=gws-wiz

# Summary

- Use in patients with HFpEF is safe but is not superior to monotherapy with valsartan in preventing CV deaths and HF related hospitalizations

# Current Recommendations for Treatment of Patients with HFpEF

## Empagliflozin in Heart Failure with a Preserved Ejection Fraction


**BACKGROUND**
Sodium–glucose cotransporter 2 inhibitors reduce the risk of hospitalization for heart failure in patients with heart failure and a reduced ejection fraction, but their effects in patients with heart failure and a preserved ejection fraction are uncertain.

**METHODS**
In this double-blind trial, we randomly assigned 5988 patients with class II–IV heart failure and an ejection fraction of more than 40% to receive empagliflozin (10 mg once daily) or placebo, in addition to usual therapy. The primary outcome was a composite of cardiovascular death or hospitalization for heart failure.

**RESULTS**
Over a median of 26.2 months, a primary outcome event occurred in 415 of 2997 patients (13.8%) in the empagliflozin group and in 511 of 2991 patients (17.1%) in the placebo group (hazard ratio, 0.79; 95% confidence interval [CI], 0.69 to 0.90; P<0.001). This effect was mainly related to a lower risk of hospitalization for heart failure in the empagliflozin group. The effects of empagliflozin appeared consistent in patients with or without diabetes. The total number of hospitalizations for heart failure was lower in the empagliflozin group than in the placebo group (407 with empagliflozin and 541 with placebo; hazard ratio, 0.73; 95% CI, 0.61 to 0.88; P<0.001). Uncomplicated genital and urinary tract infections and hypotension were reported more frequently with empagliflozin.

**CONCLUSIONS**
Empagliflozin reduced the combined risk of cardiovascular death or hospitalization for heart failure in patients with heart failure and a preserved ejection fraction, regardless of the presence or absence of diabetes. (Funded by Boehringer Ingelheim and Eli Lilly; EMPEROR-Preserved ClinicalTrials.gov number, **NCT03057951. opens in new tab**).

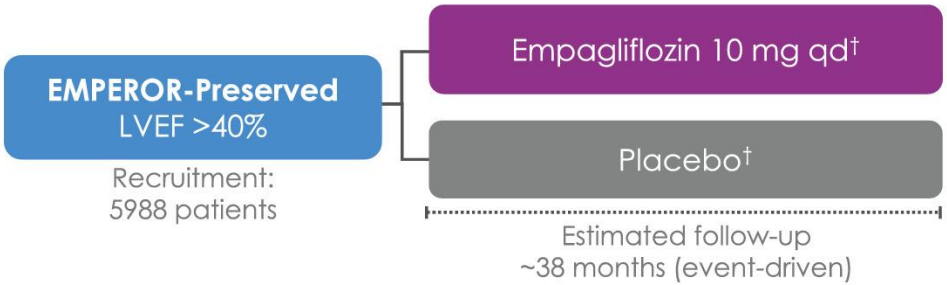
# EMPEROR PRESERVED (2021)

## EMPEROR-Preserved

### Phase III randomised double-blind placebo-controlled event driven trial

**Key Inclusion Criteria:** T2D and non-T2D, aged ≥18 years, chronic HF (NYHA class II–IV) with LVEF >40%, elevated NT-proBNP concentrations and structural heart changes or documented HHF within 12 months.

**Key Exclusion Criteria:** Symptomatic hypotension and eGFR <20 mL/min/1.73m2.




**COMPOSITE PRIMARY ENDPOINT**

Time to first event of adjudicated CV death or adjudicated HHF

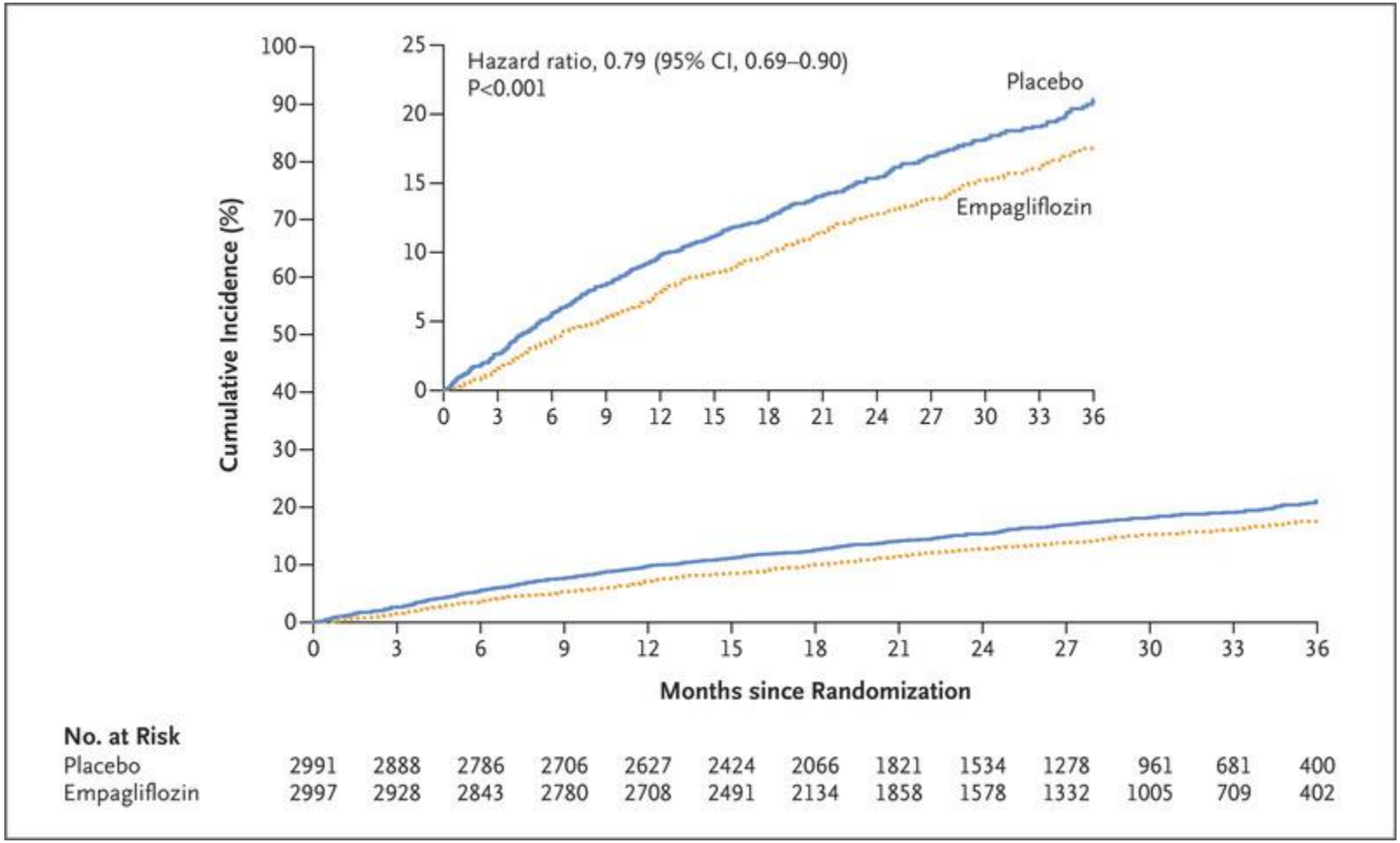
**CONFIRMATORY KEY SECONDARY ENDPOINTS**

- First and recurrent adjudicated HHF events
- Slope of change in eGFR (CKD-EPI) from baseline

†Guideline-directed medical therapy

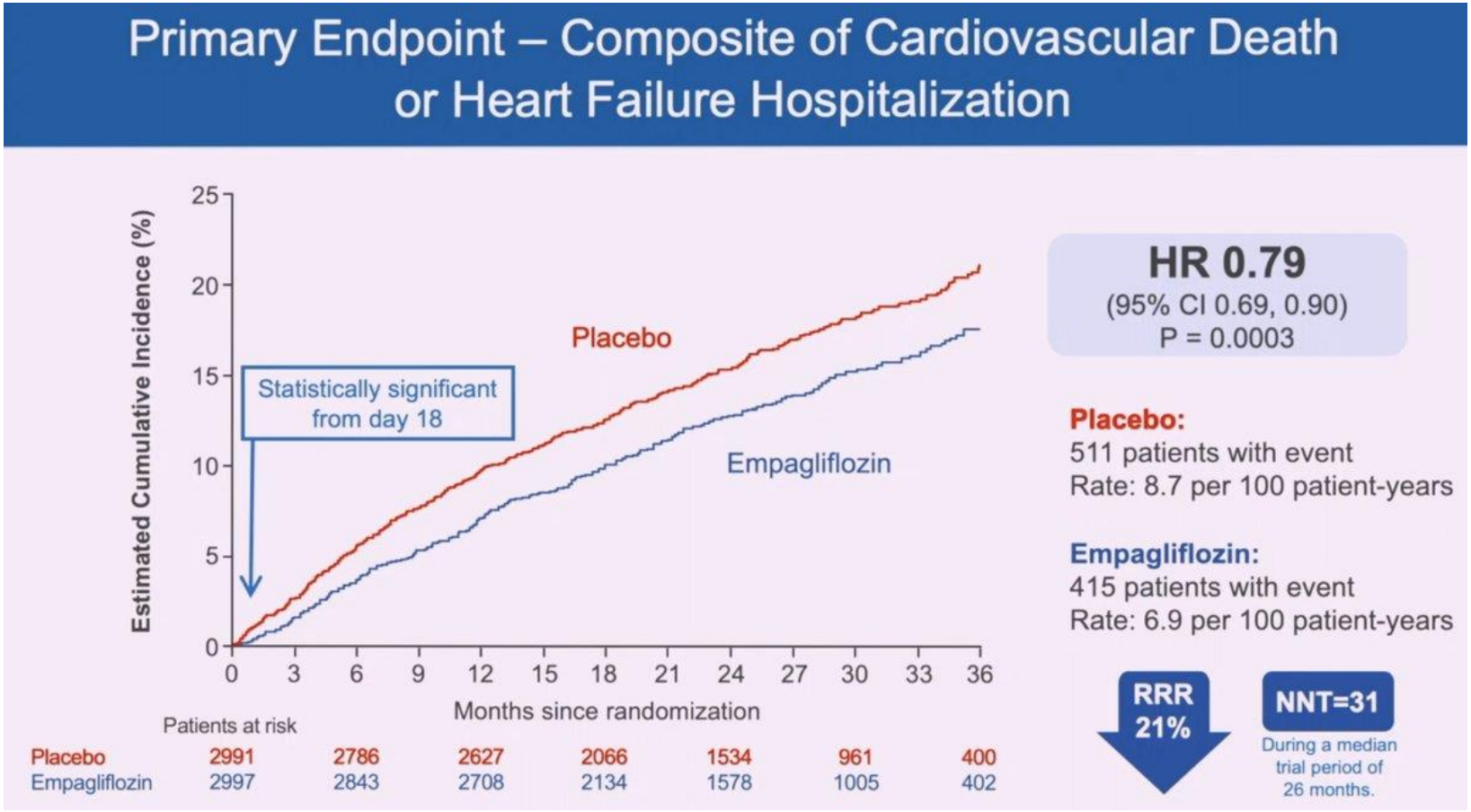
https://www.google.com/search?source=univ&tbm=isch&q=EMPERORreserved+trial+ppt+slides&fir=YqEgEc5aaU3kpM%252CX6rZG9NVDy5byM%252C_%253BIIM_iVmvlGTTwM%252Ccvdzu8A5QVSBIM%252C_%253B3Ihir97zTqsvfM%252CQHa5_uMvO-4gSM%252C_%253B3U9yGDCI27FFbM%252CaBR75Y

# EMPEROR PRESERVED (2021)




https://www.google.com/search?source=univ&tbm=isch&q=EMPERORreserved+trial+ppt+slides&fir=YqEgEc5aaU3kpM%252CX6rZG9NVDy5byM%252C_%253BIIM_iVmvlGTTwM%252Ccvdzu8A5QVSBIM%252C_%253B3Ihir97zTqsvfM%252CQHa5_uMvO-4gSM%252C_%253B3U9yGDCI27FFbM%252CaBR75Y

# EMPEROR PRESERVED (2021)




https://www.google.com/search?source=univ&tbm=isch&q=EMPERORreserved+trial+ppt+slides&fir=YqEgEc5aaU3kpM%252CX6rZG9NVDy5byM%252C_%253BIIM_iVmvlGTTwM%252Ccvdzu8A5QVSBIM%252C_%253B3Ihir97zTqsvfM%252CQHa5_uMvO-4gSM%252C_%253B3U9yGDCI27FFbM%252CaBR75Y

# EMPEROR PRESERVED (2021)

| Efficacy Outcomes | Empagliflozin | Placebo | Hazard ratio/difference (95% confidence interval) |
|---|---|---|---|
| Death from any cause | 14.1% | 14.3% | 1.00 (0.87-1.15) |
| CV death | 7.3% | 8.2% | 0.91 (0.76-1.09) |
| Death or hospitalization | 45.2% | 47.8% | **0.92 (0.85-0.99); -2.6%** |
| Total* hospitalizations for any cause | 2566 | 2768 | 0.93 (0.85-1.01) |
| Total* HF hospitalizations | 407 | 541 | **0.73 (0.61-0.88)** |
| 1° outcome (Time to 1st HF hospitalization or CV death) | 13.8% | 17.1% | **0.79 (0.69-0.90); -3.3%** |
| 1st HF hospitalization | 8.6% | 11.8% | **0.71 (0.60-0.83); -3.2%** |
| Change in KCCQ clinical summary score at 1 y | +4.5 | +3.2 | **+1.3 (+0.45 to +2.2)** |
| eGFR mean change/y | -1.25 | -2.62 | **+1.36 (+1.06-1.66)** |

**First & recurrent*

https://www.google.com/search?source=univ&tbm=isch&q=EMPERORreserved+trial+ppt+slides&fir=YqEgEc5aaU3kpM%252CX6rZG9NVDy5byM%252C_%253BIIM_iVmvlGTTwM%252Ccvdzu8A5QVSBIM%252C_%253B3Ihir97zTqsvfM%252CQHa5_uMvO-4gSM%252C_%253B3U9yGDCI27FFbM%252CaBR75Y

# PRESERVED-HF (2021)

## The PRESERVED-HF Study

Effects of Dapagliflozin on Symptoms and Functional Status in Patients With Heart Failure and Preserved Ejection Fraction

# PRESERVED-HF (2021)

## Inclusion Criteria

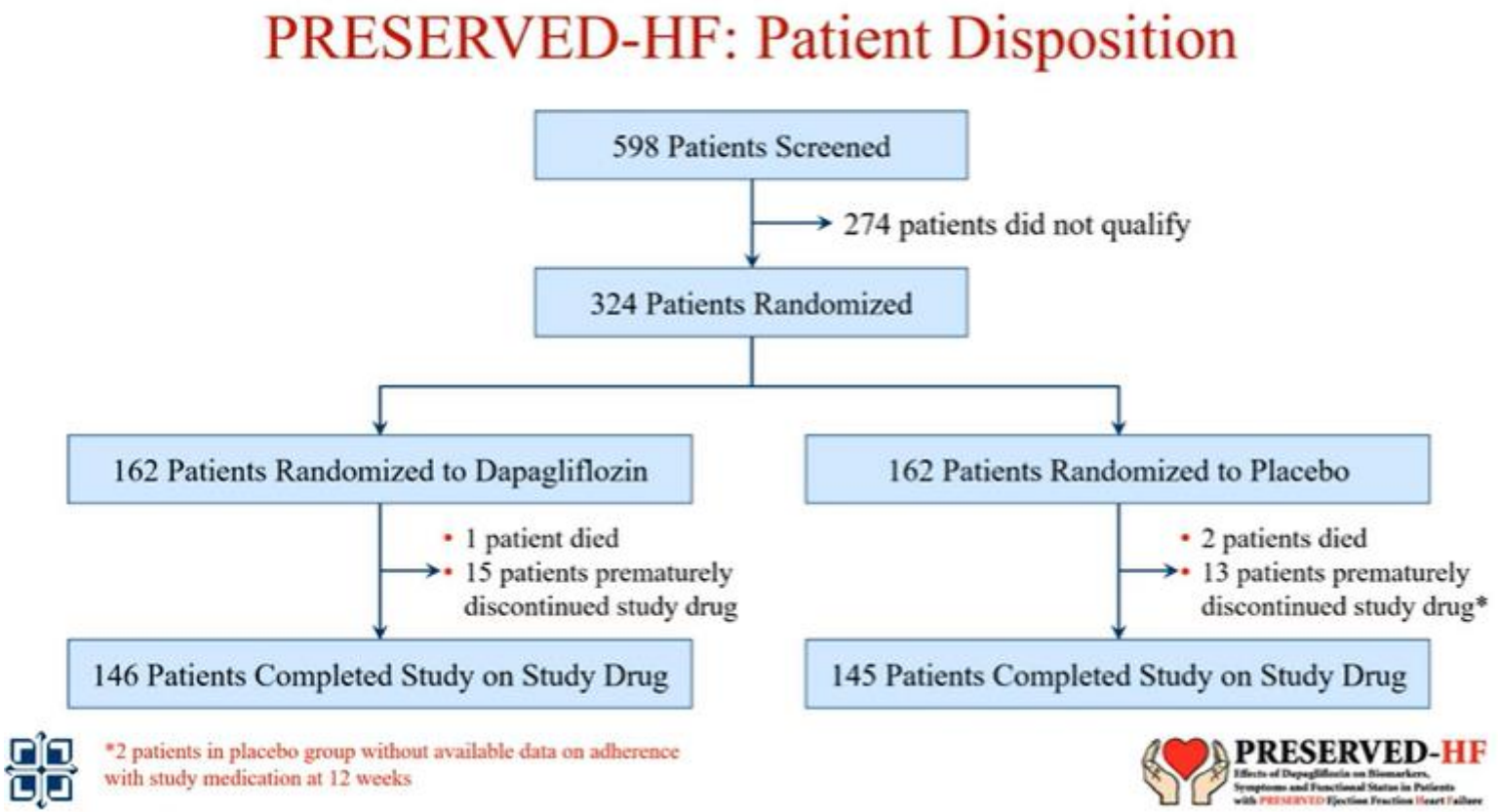
- HF with NYHA class II-IV symptoms (with or without T2D)
- Left Ventricular Ejection Fraction ≥ 45%
- NTproBNP ≥ 225 pg/mL (or BNP ≥ 75 pg/mL)*
- Requirement for diuretic therapy
- At least one of the following
  - Recent HF hospitalization or urgent HF visit requiring IV diuretic
  - Elevated filling pressures by right or left heart catheterization
  - Structural heart disease by echocardiography

*in patients with Atrial Fibrillation, NTproBNP ≥ 375 pg/mL or BNP ≥ 100 pg/mL

PRESERVED-HF
Effects of Dapagliflozin on Biomarkers, Symptoms and Functional Status in Patients with PRESERVED Ejection Fraction Heart Failure

The PRESERVED-HF Study – Main Study Presentation and Discussion | USC Journal

# PRESERVED-HF (2021)




The PRESERVED-HF Study – Main Study Presentation and Discussion | USC Journal

# PRESERVED-HF (2021)

## Baseline Characteristics

| Baseline Characteristics | Dapagliflozin (n = 162) | Placebo (n = 162) | P-Value |
|---|---|---|---|
| **Demographics** | | | |
| Age (years) | 69 (64, 77) | 71 (63, 78) | 0.44 |
| Women | 92 (57%) | 92 (57%) | 1.00 |
| White | 108 (67%) | 109 (69%) | 0.91 |
| African American | 50 (31%) | 47 (30%) | |
| **Medical History** | | | |
| Duration of Heart Failure (years) | 3.0 (1.1, 6.5) | 3.2 (1.0, 6.6) | 0.20 |
| Prior Hospitalization for Heart Failure | 98 (61%) | 83 (51%) | 0.09 |
| Ejection Fraction (%) | 60 (55, 65) | 60 (54, 65) | 0.89 |
| Ischemic Heart Disease | 32 (20%) | 31 (19%) | 0.89 |
| Type 2 Diabetes | 90 (56%) | 91 (56%) | 0.91 |
| Atrial Fibrillation | 82 (51%) | 89 (55%) | 0.44 |
| ICD | 7 (4%) | 9 (6%) | 0.61 |

PRESERVED-HF

Effects of Dapagliflozin on Biomarkers, Symptoms and Functional Status in Patients with PRESERVED Ejection Fraction Heart Failure

The PRESERVED-HF Study – Main Study Presentation and Discussion | USC Journal

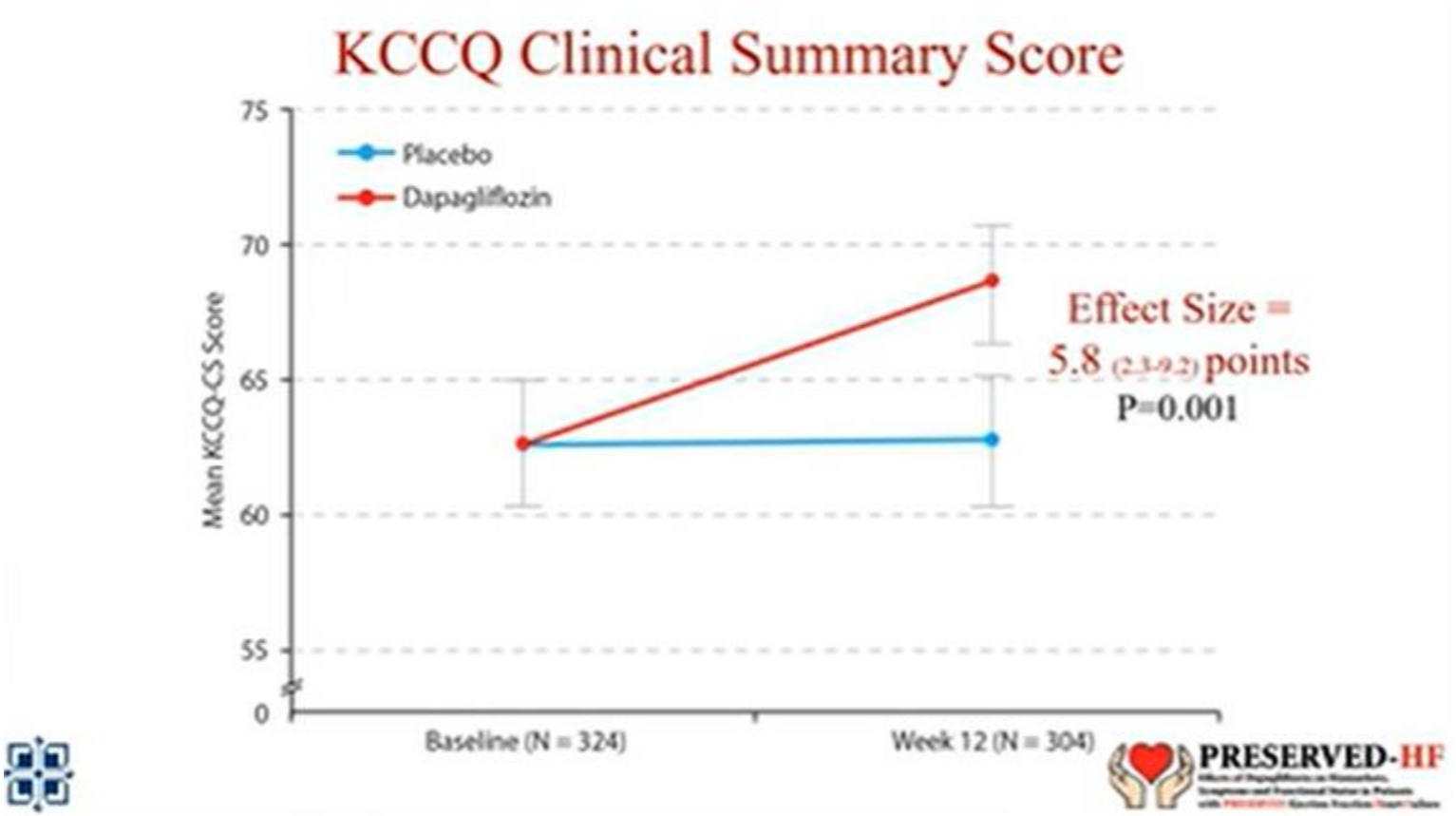
# PRESERVED-HF (2021)

## Baseline Characteristics

### *Baseline HF/CV Medications*

| Baseline Characteristics | Dapagliflozin (n = 162) | Placebo (n = 162) | P-Value |
|---|---|---|---|
| **Baseline HF/CV Medications** | | | |
| ACE Inhibitor/ARB | 98 (61%) | 98 (61%) | 1.00 |
| ARNI | 2 (1.2%) | 3 (1.9%) | |
| Beta Blockers | 119 (74%) | 116 (72%) | 0.71 |
| Hydralazine | 25 (15%) | 18 (11%) | 0.25 |
| Long Acting Nitrates | 34 (21%) | 27 (17%) | 0.32 |
| MRA | 50 (31%) | 68 (42%) | 0.04 |
| Loop Diuretics | 151 (93%) | 135 (83%) | 0.01 |
| Lipid Lowering Agents | 132 (82%) | 127 (78%) | 0.49 |
| Anticoagulant Agents | 71 (44%) | 84 (52%) | 0.15 |

# PRESERVED-HF (2021)




The PRESERVED-HF Study – Main Study Presentation and Discussion | USC Journal

# PRESERVED-HF (2021)

## Safety*

| | Dapagliflozin (n = 162) | Placebo (n = 162) |
|---|---|---|
| All reported adverse events | 44 (27%) | 38 (24%) |
| Serious adverse event | 31 (19%) | 22 (14% ) |
| Adverse events resulting in discontinuation of study medication | 18 (11%) | 15 (9%) |
| Drug adverse events | 7 (4%) | 8 (5%) |
| All cause death | 1 (0.6%) | 2 (1.2%) |
| Non-fatal MI | 0 (0%) | 1 (0.6%) |
| Stroke | 0 (0.0%) | 1 (0.6%) |
| Acute kidney injury | 5 (3%) | 5 (3%) |
| Diabetic ketoacidosis | 0 (0%) | 0 (0%) |
| Volume depletion events | 11 (7%) | 7 (4%) |
| Severe hypoglycemic events | 0 (0%) | 0 (0%) |
| Lower limb amputations | 0 (0%) | 0 (0%) |

*patients with events

PRESERVED-HF

# PRESERVED-HF (2021)

## Summary

- Dapagliflozin significantly improved symptoms and physical limitations in patients with HFpEF in just 12 weeks
- The treatment effect was large, clinically meaningful and statistically significant
- Effects were consistent across all key subgroups, including participants with and without Type 2 Diabetes, and those with ejection fraction above and below 60%
- Dapagliflozin well tolerated, with no new safety signals

# PRESERVED-HF (2021)

## What Are the Clinical Implications?

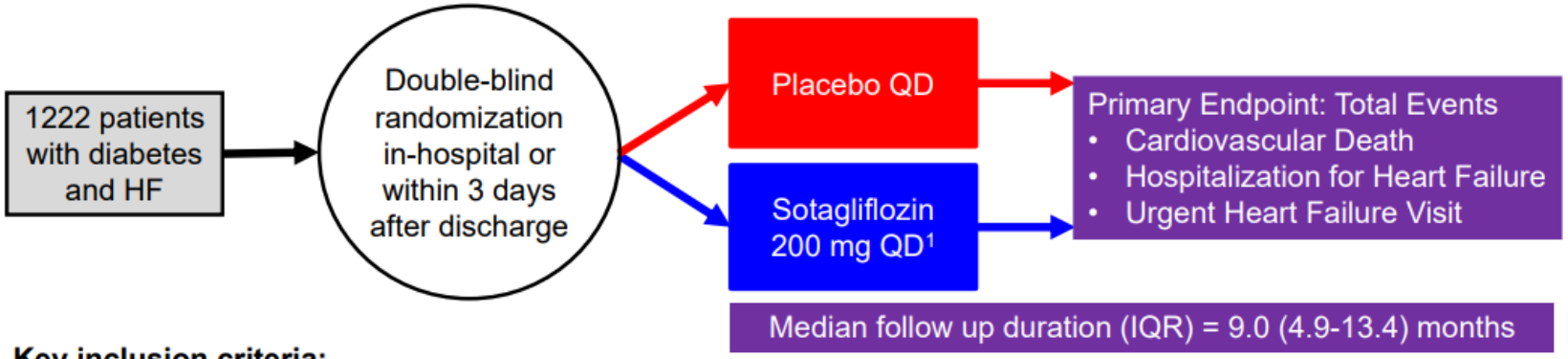
- Goals of therapy in HFpEF include reducing death and hospitalizations, and *enabling patients to feel better and do more*
- PRESERVED-HF is the first trial to demonstrate that SGLT2 inhibitor dapagliflozin significantly improves symptoms, physical limitations and 6-minute walking distance in HFpEF
  - Benefit evident at 12 weeks
- Findings highly complementary to those of large outcome trials
- Collectively, these results support the use of SGLT2 inhibitors as a new treatment option in patients with HFpEF – a morbid condition with few therapeutic options
- Important implications for guidelines, clinical practice

PRESERVED-HF
Effects of Dapagliflozin on Biomarkers, Symptoms and Functional Status in Patients with PRESERVED Ejection Fraction Heart Failure

The PRESERVED-HF Study – Main Study Presentation and Discussion | USC Journal

# SOLOIST-HF (2021)

## SOLOIST-WHF Trial Design




**Key inclusion criteria:**

- Admission with signs and symptoms of HF
- Treatment with intravenous diuretics
- Stabilized, off oxygen, transitioning to oral diuretics
- BNP ≥150 pg/mL (≥450 pg/mL if afib) or NT-proBNP ≥600 pg/mL (≥1800 pg/mL if afib)
- Type 2 diabetes

**Key exclusion criteria:**

- End-stage HF
- Recent ACS, stroke, PCI, or CABG
- eGFR <30 mL/min/1.73m$^2$

[1]Goal of dose increase to 400 mg QD

**Bhatt DL, Szarek M, Steg PG, et al., and Pitt B. *N Engl J Med.* 2020. Bhatt DL. AHA 2020, virtual.**

# SOLOIST-HF (2021)

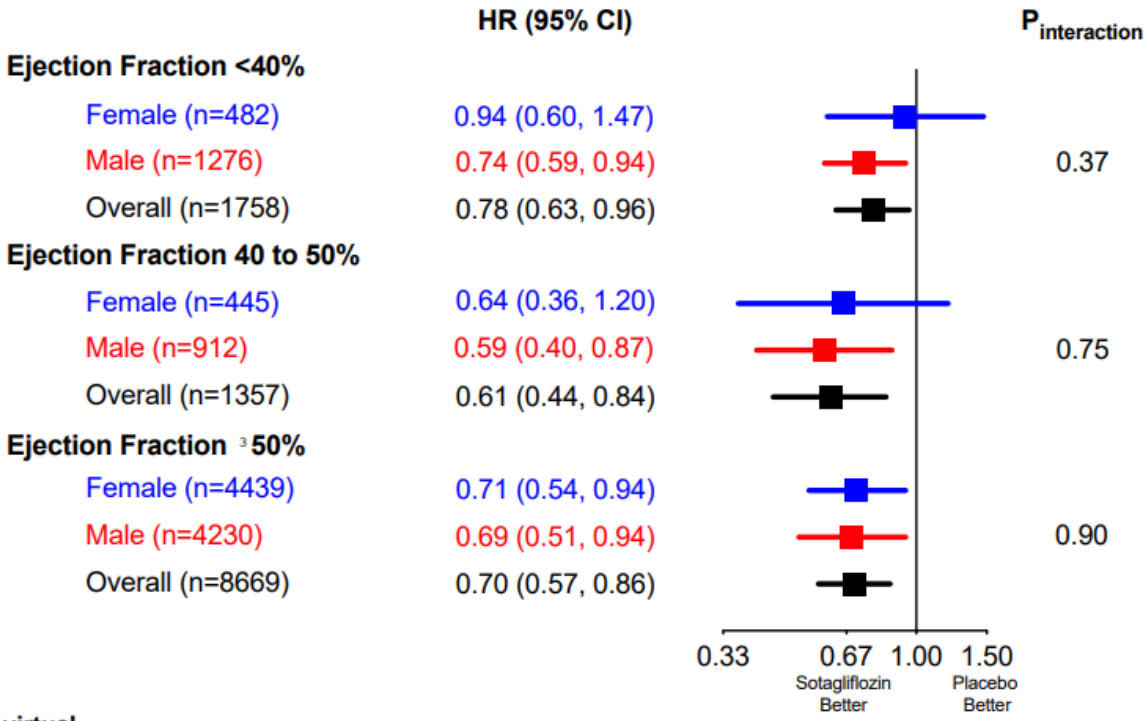
In the SOLOIST-HF trial, recently hospitalized patients with type 2 diabetes and either HFpEF (20 percent of patients) or HFrEF were randomly assigned to treatment with sotagliflozin (a combined SGLT2/SGLT1 inhibitor) or placebo

At a median follow-up of 7.7 months, the primary endpoint of cardiovascular death, hospitalization, or urgent visit for HF was lower in the sotagliflozin group (51 versus 76 events per 100 patient-years; HR 0.67, 95% CI 0.52-0.85). The effect was driven entirely by a reduction in hospitalization and urgent visits for HF (40 versus 64 events per 100 patient-years; HR 0.64, 95% CI 0.49-0.83).

# SOLOIST-HF (2021)

## Pooled Data: SOLOIST and SCORED Total CV Death, HHF, and Urgent HF Visit in 11,784 Patients

SOLOIST
SCORED




Bhatt DL. ACC 2021, virtual.

file:///C:/Users/Chad/Desktop/8amET-SOLOIST-and-SCORED-acc-2021.pdf

# SOLOIST-HF (2021)

## Conclusions

SOLOIST SCORED

**Sotagliflozin** robustly and significantly reduced the composite of total cardiovascular deaths, hospitalizations for heart failure, and urgent visits for heart failure across the full range of ejection fraction, including in patients with heart failure with preserved ejection fraction.

As well, in on-treatment analyses, **sotagliflozin** demonstrated a significant reduction in cardiovascular death.

These are the first randomized data from a prespecified analysis of clinical trials to show a significant effect of a therapy on heart failure with preserved ejection fraction, additionally demonstrating a consistent and significant benefit in women.

Bhatt DL. ACC 2021, virtual.

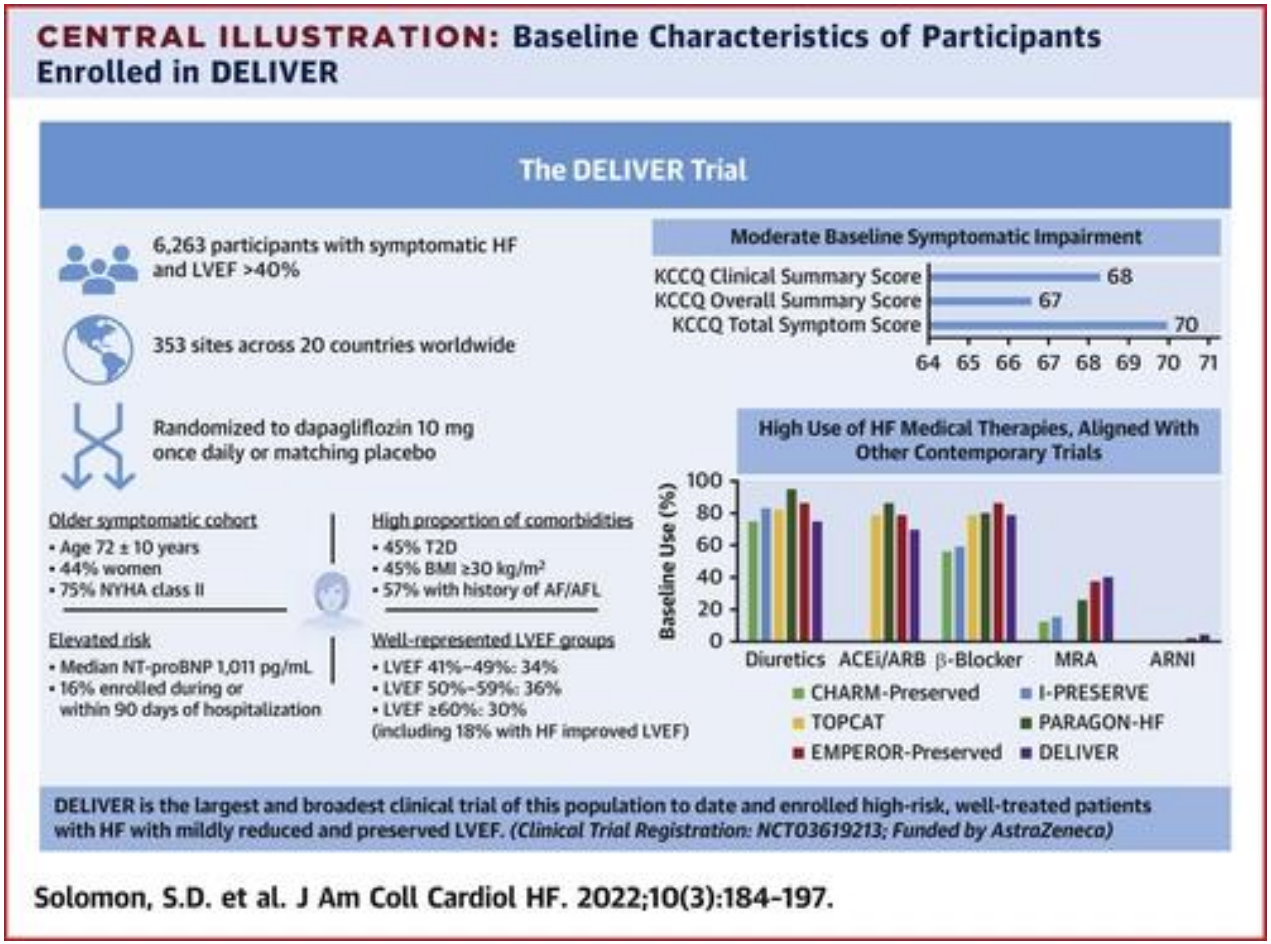
# DELIVER (2022)

**Dapagliflozin in heart failure with preserved and mildly reduced ejection fraction: rationale and design of the DELIVER trial**

Sodium–glucose co-transporter 2 (SGLT2) inhibitors, originally developed as glucose-lowering agents, have been shown to reduce heart failure hospitalizations in patients with type 2 diabetes without established heart failure, and in patients with heart failure with and without diabetes. Their role in patients with heart failure with preserved and mildly reduced ejection fraction remains unknown.

https://doi.org/10.1002/ejhf.2249

# DELIVER (2022)




https://www.jacc.org/doi/pdf/10.1016/j.jchf.2021.11.006

# DELIVER (2022)

**Dapagliflozin in heart failure with preserved and mildly reduced ejection fraction: rationale and design of the DELIVER trial**

Methods

Dapagliflozin Evaluation to Improve the LIVEs of Patients With PReserved Ejection Fraction Heart Failure (DELIVER) is an international, multicentre, parallel group, event-driven, randomized, double-blind trial in patients with chronic heart failure and left ventricular ejection fraction (LVEF) >40%, comparing the effect of dapagliflozin 10 mg once daily, vs. placebo, in addition to standard of care. Patients with or without diabetes, with signs and symptoms of heart failure, a LVEF >40%, elevation in natriuretic peptides and evidence of structural heart disease are eligible. The primary endpoint is time-to-first cardiovascular death or worsening heart failure event (heart failure hospitalization or urgent heart failure visit), and will be assessed in dual primary analyses – the full population and in those with LVEF <60%. The study is event-driven and will target 1117 primary events. A total of 6263 patients have been randomized.

https://doi.org/10.1002/ejhf.2249

# DELIVER (2022)

**Dapagliflozin in heart failure with preserved and mildly reduced ejection fraction: rationale and design of the DELIVER trial**

Conclusions

DELIVER will determine the efficacy and safety of the SGLT2 inhibitor dapagliflozin, added to conventional therapy, in patients with heart failure and preserved and mildly reduced ejection fraction.

https://doi.org/10.1002/ejhf.2249

# VITALITY-HFpEF (2022)

VITALITY-HFpEF

NCT03547583

## Vericiguat in Heart Failure with Preserved Ejection Fraction: The VITALITY-HFpEF Trial

**Trial to eValuate the efficacy and safeTy of the orAL sGC stImulator vericiguaT to improve phYsical functioning in activities of daily living in patients with HFpEF**

Paul W. Armstrong, MD, Carolyn S.P. Lam, MD, Kevin J. Anstrom, PhD, Justin Ezekowitz, MBBCh, Adrian F. Hernandez, MD, MHS, Christopher M. O'Connor, MD, Burkert Pieske, MD, Piotr Ponikowski, MD, PhD, Sanjiv J. Shah, MD, Scott D. Solomon, MD, Adriaan A. Voors, MD, Lilin She, PhD, Vanja Vlajnic, MS, MAS, Francine Carvalho, MD, PhD, Luke Bamber, MSc, Robert O. Blaustein, MD, PhD, Lothar Roessig, MD, and Javed Butler, MD, MPH, MBA
on behalf of the VITALITY-HFpEF Study Group

Canadian VIGOUR Centre
Bridging Hearts and Minds

Duke Clinical Research Institute

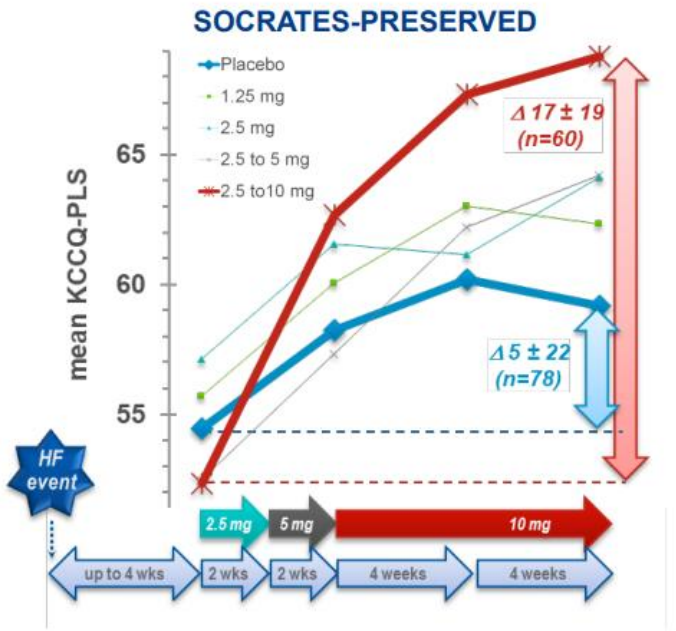
https://thecvc.ca/wp-content/uploads/2017/01/VITALITY_Primary_HFA-Discovery_June-12-2020-Session_FINAL.pdf

# VITALITY-HFpEF (2022)

## sGC and Physical Function in HFpEF

- Patients with HFpEF have substantially reduced functional capacity and quality of life[1]
- No treatment exists to address this major unmet need[2]
- Physiologic stimulation of sGC by NO is disrupted in HFpEF due to comorbidity-related inflammation[3]
- Soluble guanylate cyclase (sGC) has a unique mechanism enhancing heart, vessel, muscle, and renal function

- **SOCRATES-PRESERVED suggested improvement in KCCQ-PLS with vericiguat in HFpEF**




D mean ± standard deviation
Full analysis set excluding subjects with incorrectly assigned doses
Filippatos et al. Eur J Heart Fail. 2017 Jun;19(6):782-791

[1] Butler et al. *Circ Heart Fail.* 2016 Nov;9(11)
[2] Yancy CW et al. *J Am Coll Cardiol.* 2017 Aug 8;70(6):776-803
[3] Shah S et al. *Circulation.* 2016;134:73-90

Canadian VIGOUR Centre
Bridging Hearts and Minds

Duke Clinical Research Institute

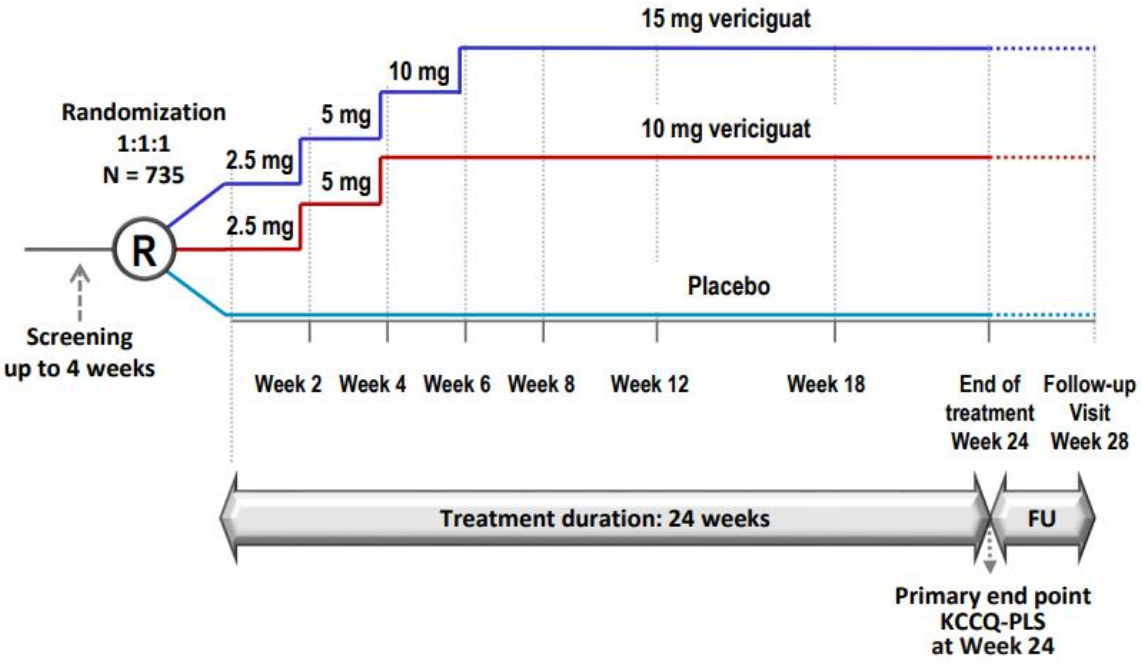
https://thecvc.ca/wp-content/uploads/2017/01/VITALITY_Primary_HFA-Discovery_June-12-2020-Session_FINAL.pdf

# VITALITY-HFpEF (2022)

## VITALITY Study Design

VITALITY -HFpEF

Previous diagnosis of chronic HF
HF event within 6mos
Elevated NT-proBNP/BNP
EF ≥45%
And
LVH and/or LAE
NYHA class II/III




Canadian VIGOUR Centre
Bridging Hearts and Minds

Duke Clinical Research Institute

https://thecvc.ca/wp-content/uploads/2017/01/VITALITY_Primary_HFA-Discovery_June-12-2020-Session_FINAL.pdf

# VITALITY-HFpEF (2022)

## Summary

- Vericiguat in target doses of 10 and 15 mg did not improve the primary outcome of KCCQ PLS nor the secondary outcome of 6-minute walking distance in a typical HFpEF population.
- Tendency for more symptomatic hypotension& syncope with both 10 and 15 mg doses suggests a pharmacodynamically active dose studied.
- Although there were more CV deaths in the vericiguat groups, the limited duration of follow up and numbers are too small for definitive conclusions.

Canadian VIGOUR Centre
Bridging Hearts and Minds

Duke Clinical Research Institute

https://thecvc.ca/wp-content/uploads/2017/01/VITALITY_Primary_HFA-Discovery_June-12-2020-Session_FINAL.pdf

# VITALITY-HFpEF (2022)

## Conclusion

- In the VITALITY-HFpEF trial, vericiguat (10 or 15 mg) compared with placebo did not improve KCCQ PLS scores or 6MWD.
- SOCRATES PRESERVED findings were not confirmed in larger population studied with two doses for a longer time
- VITALITY aligned with prior studies of the NO-sGC-cGMP pathway that did not improve HFpEF
- Further studies are needed to identify effective interventions to improve outcomes in patients with HFpEF

Canadian VIGOUR Centre
Bridging Hearts and Minds

Duke Clinical Research Institute

https://thecvc.ca/wp-content/uploads/2017/01/VITALITY_Primary_HFA-Discovery_June-12-2020-Session_FINAL.pdf

# FINEARTS-HR (2024)

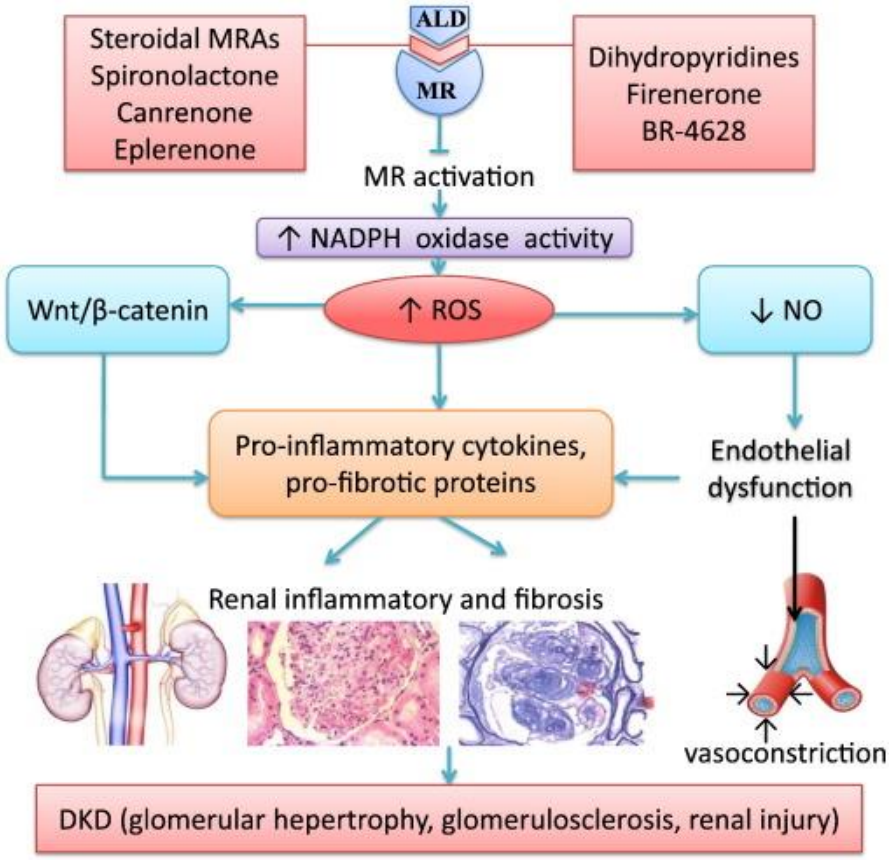
**Study to Evaluate the Efficacy (Effect on Disease) and Safety of Finerenone on Morbidity (Events Indicating Disease Worsening) & Mortality (Death Rate) in Participants With Heart Failure and Left Ventricular Ejection Fraction (Proportion of Blood Expelled Per Heart Stroke) Greater or Equal to 40% (FINEARTS-HF)**

Study to Evaluate the Efficacy (Effect on Disease) and Safety of Finerenone on Morbidity (Events Indicating Disease Worsening) & Mortality (Death Rate) in Participants With Heart Failure and Left Ventricular Ejection Fraction (Proportion of Blood Expelled Per Heart Stroke) Greater or Equal to 40% - Full Text View - ClinicalTrials.gov

# FINEARTS-HR (2024)

## Finerenone mechanism of action

Finerenone is a selective antagonist of the mineralocorticoid receptor (MR). **Activated by aldosterone and cortisol, the nonsteroidal MRA regulates gene transcription**. The overexpression of the MR is believed to contribute to fibrosis and inflammation




Study to Evaluate the Efficacy (Effect on Disease) and Safety of Finerenone on Morbidity (Events Indicating Disease Worsening) & Mortality (Death Rate) in Participants With Heart Failure and Left Ventricular Ejection Fraction (Proportion of Blood Expelled Per Heart Stroke) Greater or Equal to 40% - Full Text View - ClinicalTrials.gov

# Summary

In patients with HFpEF (LVEF ≥50 percent) who have New York Heart Association (NYHA) class II to III symptoms and who have an elevated B-type natriuretic peptide level (BNP; ie, BNP >100 pg/dL or N-terminal pro-BNP [NT-proBNP] >300 pg/dL).

Recommend treatment with both a sodium-glucose co-transporter 2 (SGLT2) inhibitor and a mineralocorticoid receptor antagonist (MRA) rather than no HFpEF-specific therapy, either treatment alone, or other agents (eg, sacubitril-valsartan, angiotensin converting enzyme [ACE] inhibitors).

# Summary

In patients with preexisting therapies for diabetes and/or chronic kidney disease (CKD) is guided by the following general principles:

-Recommend starting an SGLT2 inhibitor first and then add the MRA two weeks later if the patient tolerates initial therapy.

-Consider monotherapy if HF symptoms resolve or if the BNP decreases in response to initial therapy.

No direct data to suggest that use of both therapies has an additive effect in reducing the risk of HF hospitalization.

# Summary

Regardless of which agent is used first, monitor for intolerance to the initial agent for approximately two weeks before starting a second agent.

In patients in whom starting an SGLT2 inhibitor or an MRA would interfere with an existing treatment, start a HFpEF-specific therapy if the benefit of the HFpEF-specific therapy is greater than the benefit of the therapy that it would replace.

The need to consider this tradeoff is commonly encountered in patients with diabetes and/or CKD

# Thank You For Your Attention!