NW Hospital Medicine: Literature Updates

Ayako Mayo, MD

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Learning Objectives

- Recognize role of GLP-1 agonists for patients with obesity and heart failure with preserved ejection fraction
- Identify appropriate duration of antibiotics for bacteremia
- Review evidence-based medical therapies for patients with heart failure with preserved ejection fraction

Disclosures

- None

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Question 1:

You admit a 55 yo woman with HFpEF, OSA, obesity (BMI 37), CKD, Type 2 diabetes for acute decompensated heart failure. She takes torsemide, insulin, dapagliflozin, and reports adherence to CPAP. What new medication should be recommended at discharge?

1. Spironolactone
2. Semaglutide
3. Lisinopril
4. Entresto (Sacubitril-Valsartan)

The NEW ENGLAND JOURNAL of MEDICINE

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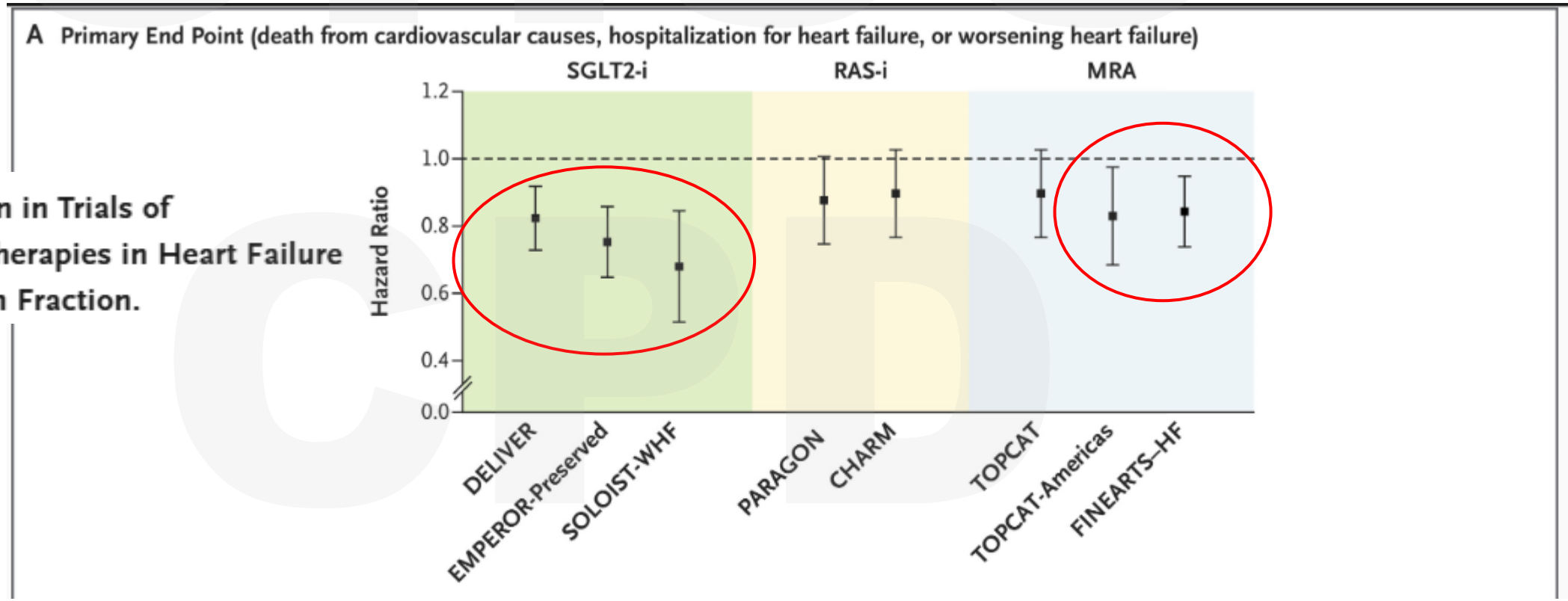
Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity

M.N. Kosiborod, S.Z. Abildstrøm, B.A. Borlaug, J. Butler, S. Rasmussen, M. Davies, G.K. Hovingh, D.W. Kitzman, M.L. Lindegaard, D.V. Møller, S.J. Shah, M.B. Treppendahl, S. Verma, W. Abhayaratna, F.Z. Ahmed, V. Chopra, J. Ezekowitz, M. Fu, H. Ito, M. Lelonek, V. Melenovsky, B. Merkely, J. Núñez, E. Perna, M. Schou, M. Senni, K. Sharma, P. Van der Meer, D. von Lewinski, D. Wolf, and M.C Petrie, for the STEP-HFpEF Trial Committees and Investigators*

Why is this Important?

- No available therapies have been shown to reduce mortality in HFpEF
- Medications improving QOL in HFpEF are limited

Treatment Effect Shown in Trials of Recommended Drug Therapies in Heart Failure with Preserved Ejection Fraction.



Why is this Important?

- HFpEF often associated with metabolic derangement and a high prevalence of obesity and diabetes
- Emerging data that medications that target obesity help reduce heart-failure symptoms and improve QOL

Design: STEP HFpEF

- Multicenter, international
- Randomized
- Controlled

- **Size**: 529 patients
- **Duration**: 52 weeks
- **Interventions**: (A) Once weekly semaglutide injections versus (B) Placebo
- **Inclusion Criteria**:
  - Patients with HFpEF with a BMI ≥ 30
- **Exclusion Criteria:**
  - History of diabetes or patient-reported weight change > 5 kg within 90 days

- Hypothesis: Semaglutide can improve QOL and reduce HF-related symptoms in patients with HFpEF

Patient Characteristics: STEP HFpEF

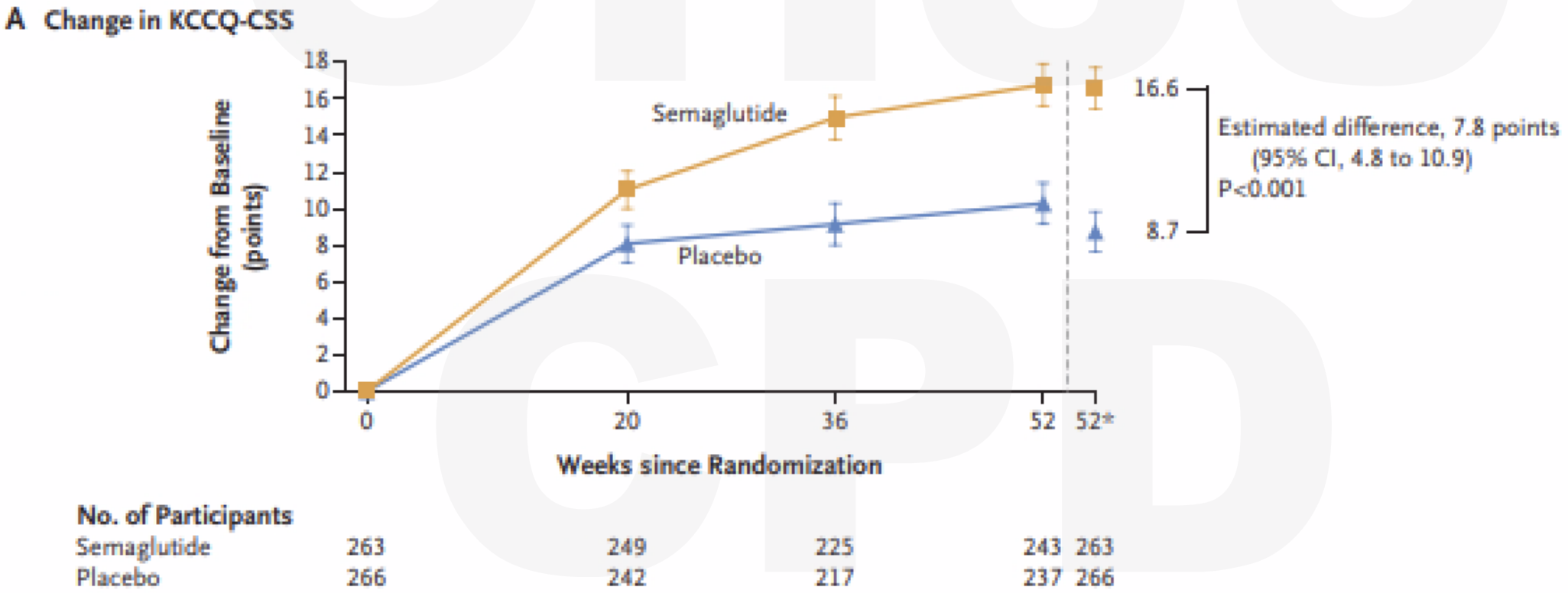
- **Median age:** 70 years
- **Gender:** 57% female, 43% male
- Race:
  - Black 3%
  - White 97%
  - ‘Other’ 0%
- **Median body weight:** 105 kg
- **Median BMI:** 37

- **Concomitant medications:**
  - Diuretic 80%
  - MRA 35%
  - ACEI, ARB, or ARNI 80%
  - Beta-blocker 79%
  - SGLT2 inhibitor 3.6%

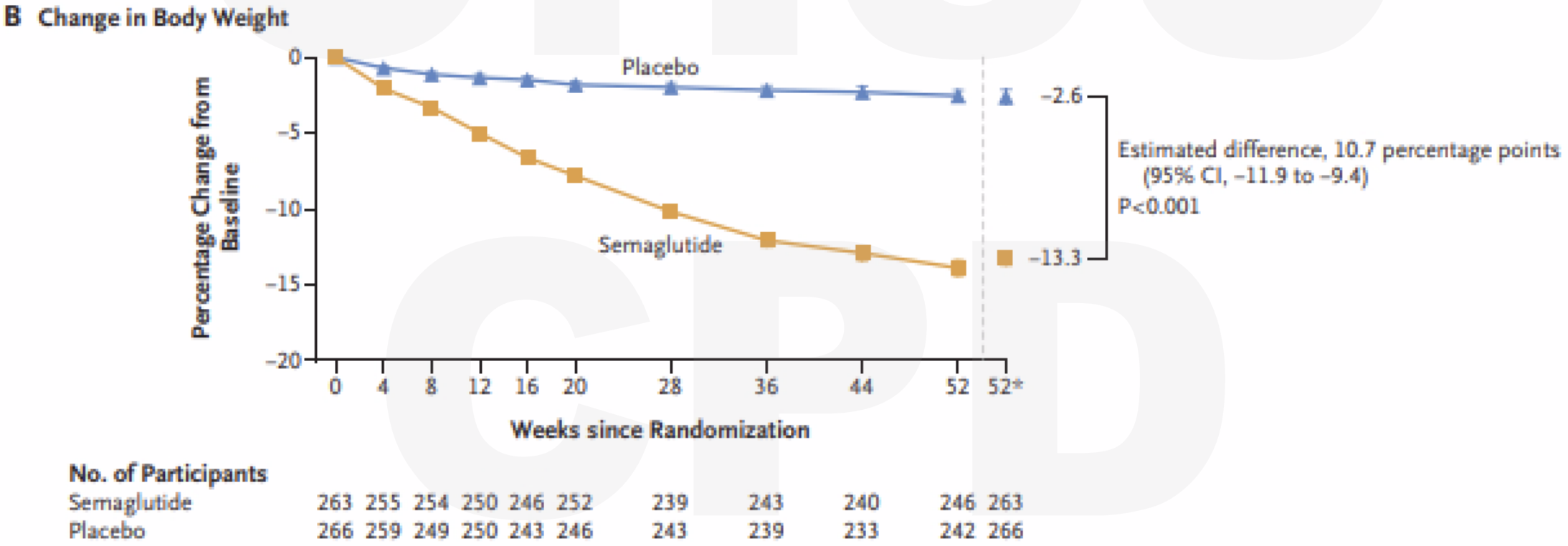
Outcomes: STEP HFpEF

- **Primary Outcome:**
  - Change in Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (change in baseline to week 52)
  - Percentage Change in Body Weight

Outcomes: STEP HFpEF



Outcomes: STEP HFpEF



Conclusions:

- The mean change in KCCQ-CSS and change in body weight were significantly greater with semaglutide than with placebo

Limitations:

- Non-White participants was low
- Trial not powered to evaluate semaglutide effects on hospitalizations
- Excluded patients with diabetes

Personal Take – Practice changing - If patient's insurance will cover, I would prescribe

Doh!

But your patient has diabetes!

And patients with HFpEF and DM? BONUS: STEP-HFpEF DM Trial

- **Patients:** Preexisting HFpEF, BMI ≥ 30, Type II diabetes
- **Intervention:** Weekly semaglutide (2.4 mg) v placebo
- **Outcome:** Superior to placebo in difference in KCCQ-CSS and weight loss
- **Follow-Up:** 52 weeks
- **Recommendation:** Initiate semaglutide in patients with HFpEF and diabetes

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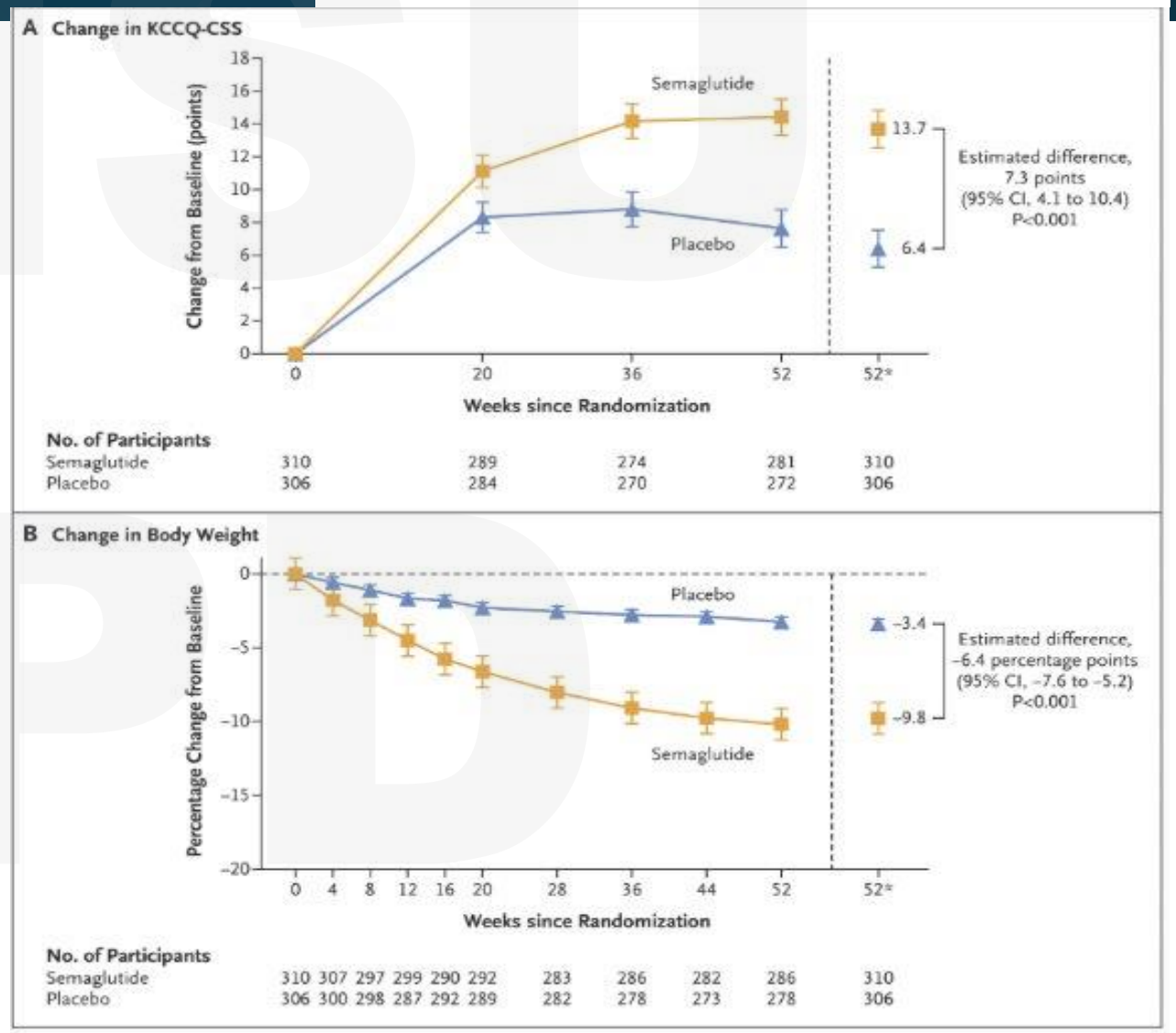
ORIGINAL ARTICLE

Semaglutide in Patients with Obesity-Related Heart Failure and Type 2 Diabetes



Question 2: She's Back

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Your patient is unfortunately back in the ED after developing fevers at home over the holiday weekend. She's also had increased urinary frequency and burning. She woke up in the middle of the night with chills and decided to come to the ED. She's febrile to 102, HR 100s, BP 137/69. Blood cultures collected while she was in ED obs are 2/2 positive for E coli. She's started on ceftriaxone and admitted to your service. After 1-2 days her sepsis has resolved. Susceptibilities showing pan-S. How do you elect to treat her?

a) Vanc and pip/tazo until her urine cultures are clear. Let's not take any chances here.

b) Switch her to PO and plan to treat for 14 days

c) Switch her to PO and plan to treat for 10 days

d) Switch her to PO and plan to treat for 7 days

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ORIGINAL ARTICLE

Antibiotic Treatment for 7 versus 14 Days in Patients with Bloodstream Infections

The BALANCE Investigators, for the Canadian Critical Care Trials Group, the Association of Medical Microbiology and Infectious Disease Canada Clinical Research Network, the Australian and New Zealand Intensive Care Society Clinical Trials Group, and the Australasian Society for Infectious Diseases Clinical Research Network

Why is this Important?

- Emerging evidence that we are likely treating too long with antibiotics
- Risks of prolonged antibiotic course – C diff infection, development of resistance, $$$

Hypothesis: 7 days of antibiotics is non-inferior to 14 days treatment in patients with bacteremia with regards to death after 90 days from all causes

Design: BALANCE

- Open-label
- Randomized
- Controlled

- Noninferiority
- International and multicenter (74 hospitals, 7 countries

- **Size:** 3,608 hospitalized patients
- **Duration:** 2014-2023
- **Interventions:** (A) 7 days versus (B) 14 days of antibiotics
  - Antibiotic (selection, dosing, route) left to discretion of treatment team

- **Inclusion Criteria:**
  - Admitted patients (med/surg and ICU) with bloodstream infection

- **Exclusion Criteria:**
  - Severely immunocompromised, prosthetic heart valve or endovascular grafts, infection requiring extended treatment (e.g. endocarditis, osteomyelitis), positive culture with a contaminant (e.g. coagulase-negative staph), S aureus or S. lugdunensis bacteremia

Patient Characteristics: BALANCE

- **Median age:** 70 years
- **Gender:** 47% female, 53% male
- **Inpatient Status:**
  - ICU: 55%
  - Non-ICU: 45%
- **Source of bacteremia:**
  - Urinary tract 42%
  - Intraabdominal or hepatobiliary 19%
  - Lung 13%
  - Skin, soft tissue 5%
  - Other/Unknown 15%
- **Number/Type of Organisms:**
  - Monomicrobial, gram-neg: 71%
  - Monomicrobial, gram-pos 18%
  - Polymicrobial 11 %
- **Most common pathogens:**
  - E coli 44%
  - Klebsiella spp 15%
  - Enterococcus spp 15%
  - Coagulase-negative staph 5%
  - Pseudomonas spp 5%
  - Strep pneumoniae 4.5%
  - Enterobacter spp 4.4%
  - Proteus spp 3.5%
  - Serratia spp 2%
  - S. pyogenes 2%
  - S. agalactiae 2%

Outcomes: BALANCE

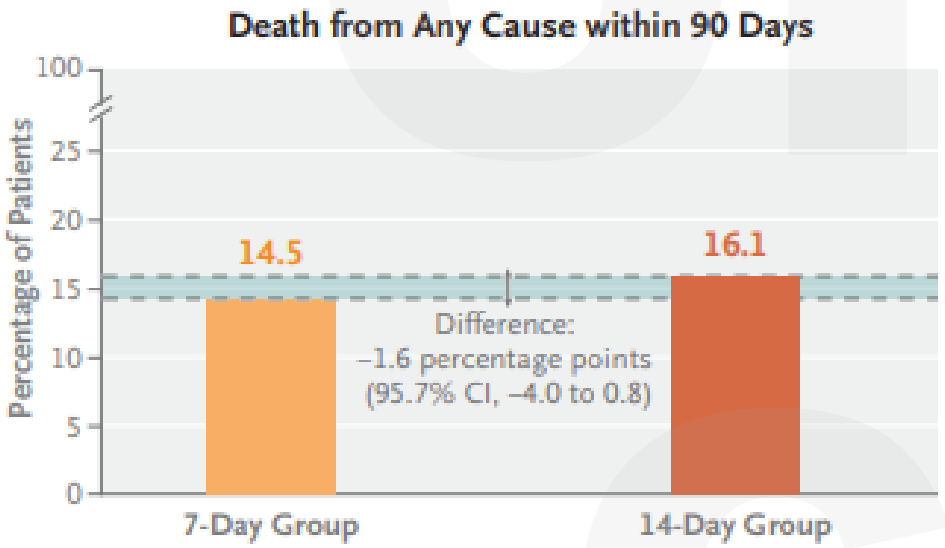
Primary:

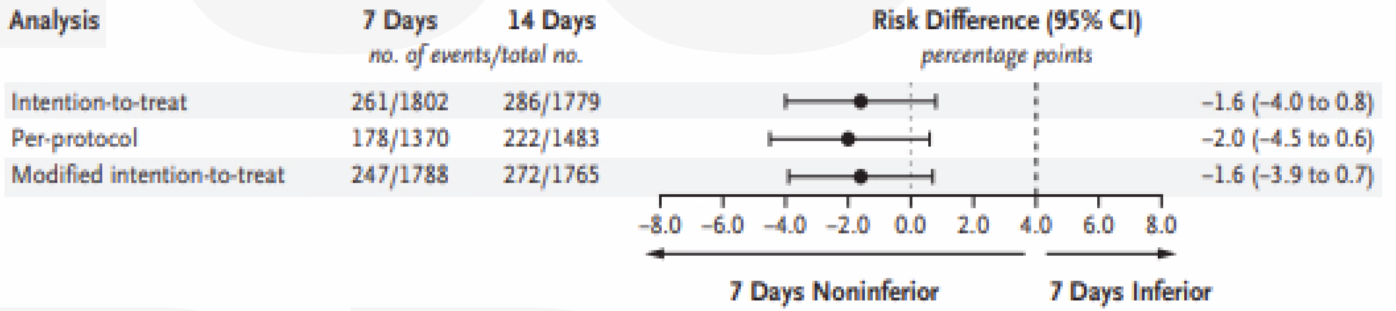
- Death from Any Cause 90 days after bloodstream infection diagnosis

Secondary:

- Death in hospital
- Death in ICU
- Relapse of bacteremia with same organism
- Adverse events (e.g. allergy, AKI)
- C diff infection in hospital

Outcomes: BALANCE





- Among hospitalized patients with bloodstream infection, antibiotic treatment for 7 days was **noninferior** to treatment for 14 days with respect to death within 90 days after diagnosis

Conclusions:

- Among hospitalized patients with bloodstream infection, antibiotic treatment for 7 days was **noninferior** to treatment for 14 days with respect to death within 90 days after diagnosis

Limitations:

- No placebo
- 23% of 7-day treatment group received antibiotics longer than 7 days
- Can’t apply to S. aureus infections or commonly seen syndromes in practice (endocarditis, osteomyelitis)

Personal Take – Practice affirming for me, would not routinely prescribe 14 days of antibiotics for uncomplicated bacteremia

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Question 3:

A 63 yo M with obesity, type 2 diabetes, HTN is admitted for DOE, peripheral edema. TTE shows LV EF of 50%. In addition to diuresis, what medication would be most appropriate to start next?

1. Semaglutide
2. Empagliflozin
3. Finerenone
4. Spironolactone

The NEW ENGLAND JOURNAL of MEDICINE

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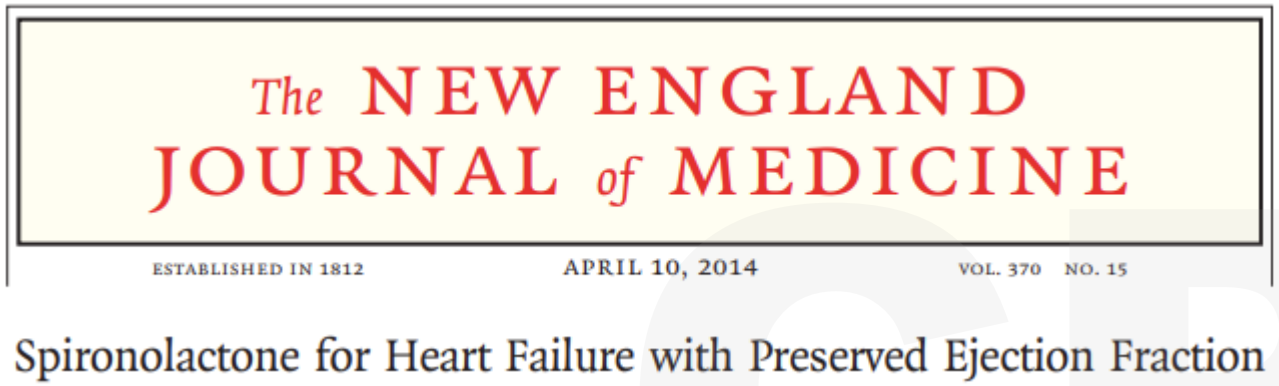
Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

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

Why Is this Important?

- No great therapy options for patients with HFpEF

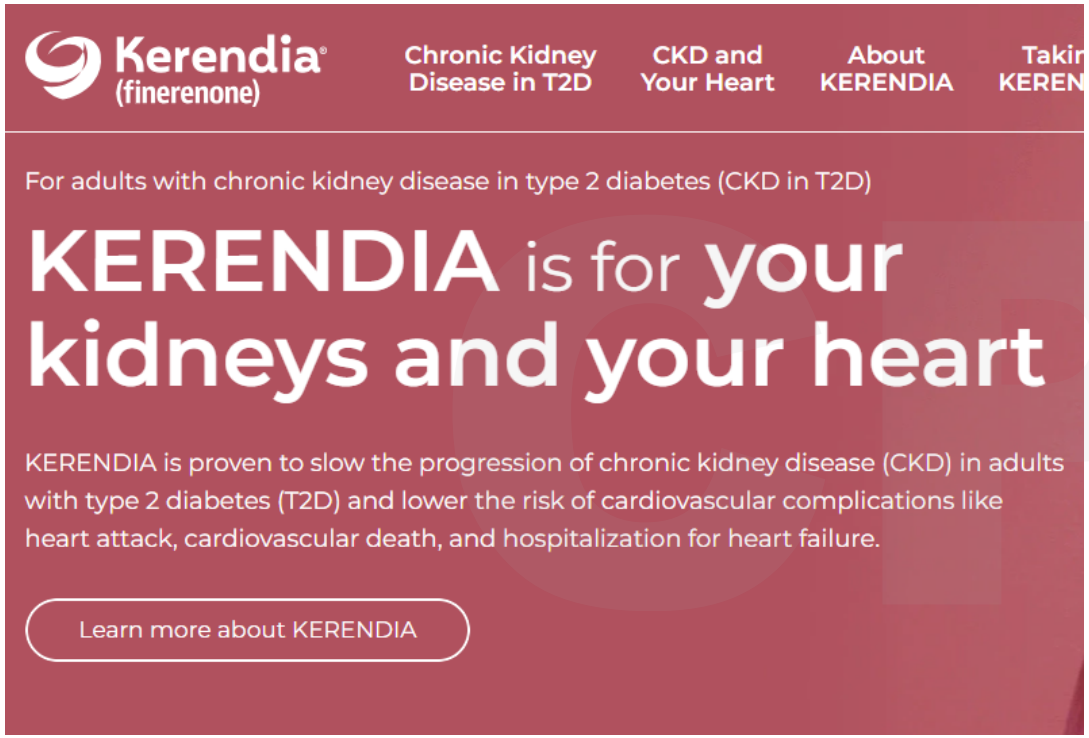


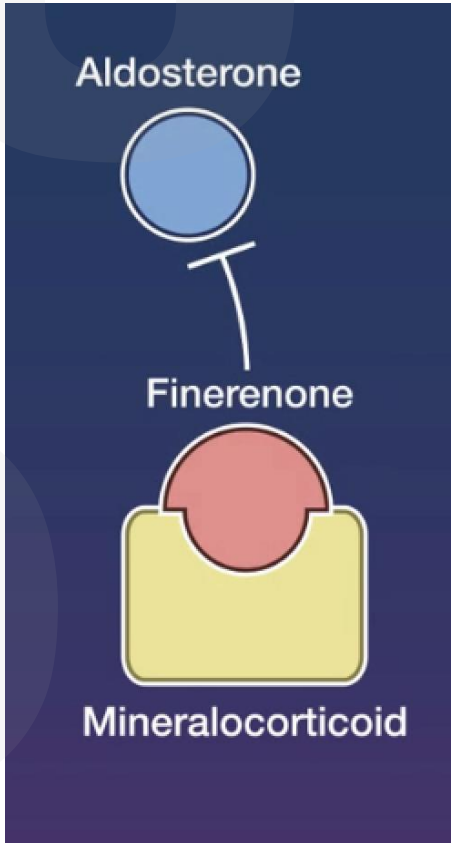
TOPCAT trial:

- Patients with EF>45% randomized to spironolactone or placebo
- No reduction in outcome of death from CV causes or hospitalization for heart failure

Finerenone?

Nonsteroidal mineralocorticoid receptor antagonist





Methods: FINEARTS-HF

- Double-blind
- Randomized
- Multi-center, international

- **Size:** ~6,000 patients
- **Duration:** 32 months
- **Interventions:**
  - Finerenone (20 v 40 mg) versus placebo (usual care)

- **Inclusion Criteria:**
  - >40 yo, symptomatic HF w EF>40%
- **Exclusion Criteria:**
  - GFR<25, K>5

Hypothesis: Finerenone, in addition to usual therapy, reduces rate of total worsening HF events and deaths from CV causes in patients with heart failure and mildly reduced or preserved EF.

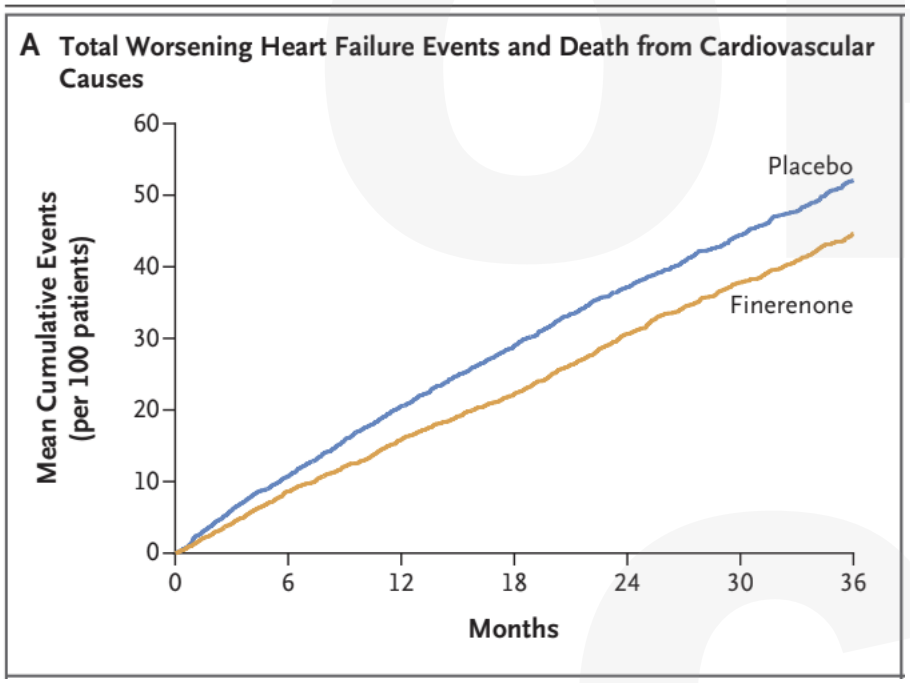
Patient Characteristics: FINEARTS-HF

- **Median age:** 72 years
- **Gender:** 45% female
- **Race:**
  - Asian 16.6%
  - Black 1.6%
  - Other 3%
  - White 78.8%
- **Previous CHF admission:** 60%
- HTN – 88% patients
- Type II DM - 41%

Outcomes: FINEARTS-HF

- **Primary:**
  - Total worsening HF events* and CV death
    - * Hospitalization related to CHF, urgent visit for CHF
- **Secondary:**
  - Total worsening HF events
  - Any death
  - NYHA functional class
  - Kidney composite outcome
  - Kansas City Cardiomyopathy Questionnaire (KCCQ) - delta

Outcomes: FINEARTS-HF



Primary Outcome:

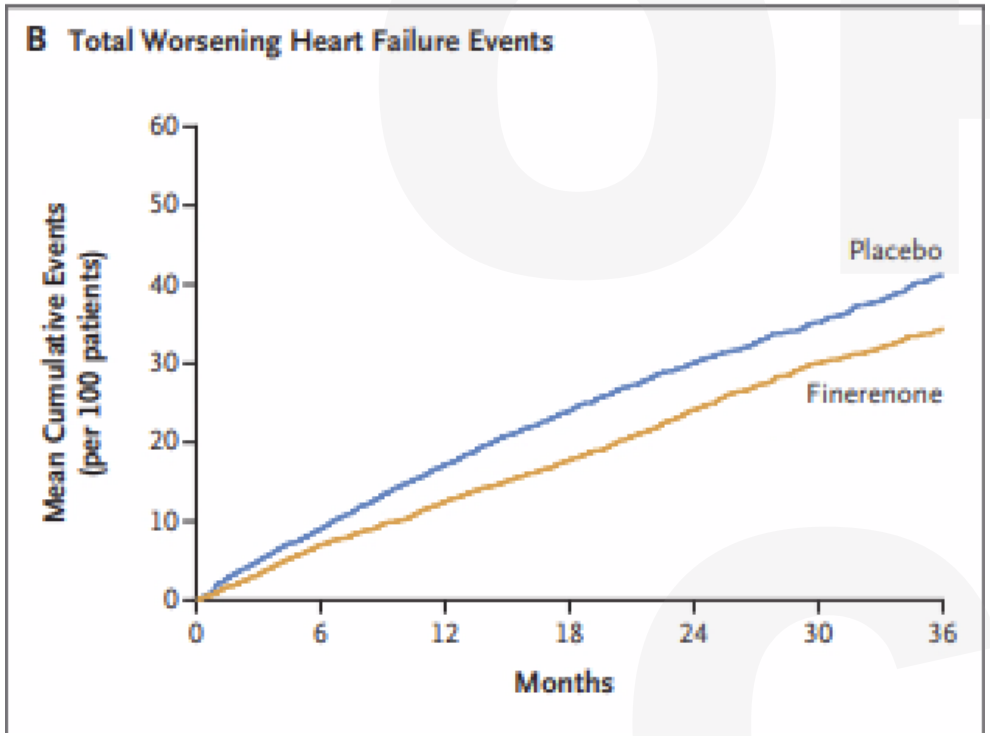
Total worsening HF events and death from CV causes:

- Finerenone: 1038 events; 14.9 per 100 patient-year
- Placebo 1283 events; 17.7 per 100 patient-year
- Rate ratio: 0.84 (95% CI, 0.74-0.95), p-value 0.007

Secondary Outcomes:

- Change in baseline KCCQ: 8 (finerenone) v 6.4 (placebo); p-value <0.001
- Improvement in NYHA class at 12 mo: OR 1.01 (0.88-1.15)
- Kidney composite outcome: HR 1.33 (0.94-1.89)
- Death from any cause : HR 0.93 (0.83-1.06)

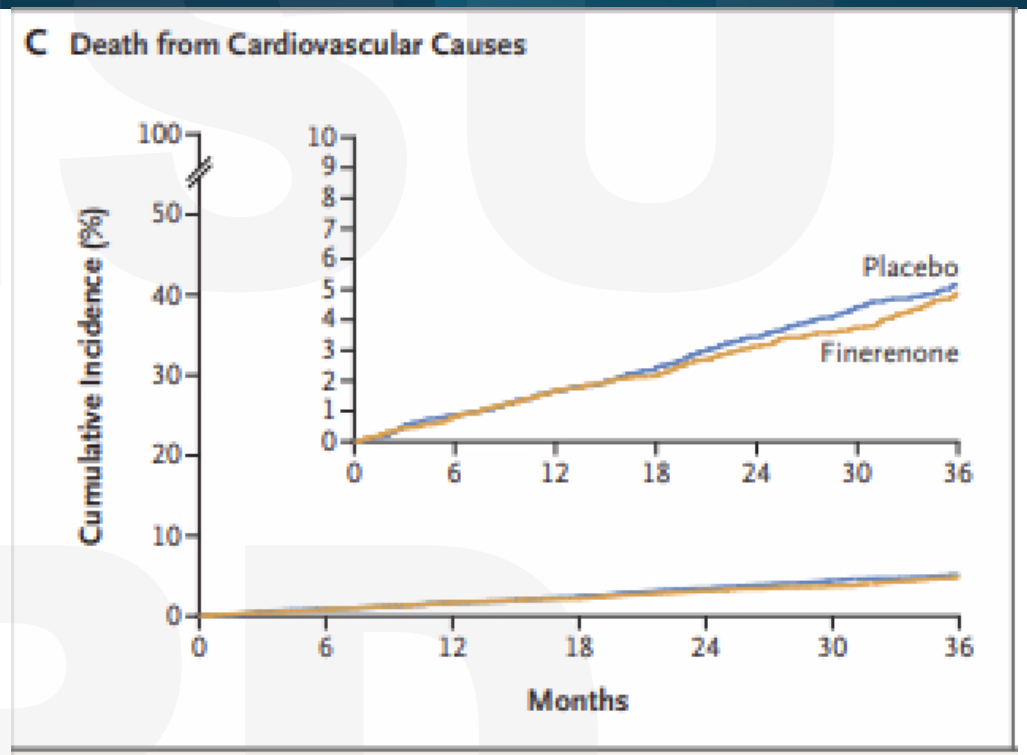
Outcomes: FINEARTS-HF



Secondary Outcome:

Total Worsening Heart Failure Events:

- Finerenone: 842 events
- Placebo 1024 events
- Rate ratio: 0.82 (95% CI, 0.71-0.94), p-value 0.006



Secondary Outcome:

Death from CV Causes:

- Finerenone: 242 events (8.1%)
- Placebo 260 events (8.7%)
- Hazard ratio: 0.93 (95% CI, 0.78-1.11)

Adverse Events

- Finerenone associated with
  - Increased risk of hyperkalemia (9.7% v 4.2%)
  - Decreased risk of hypokalemia (<3.5mmol/liter) (4.4% v 9.7%)

Conclusions

In patients with HF and mildly reduced or preserved EF, finerenone resulted in a significantly lower rate of a composite of total worsening heart failure events and death from CV causes as compared to placebo

Limitations:

- The trial enrolled few Black patients
- Benefits of finerenone can’t be generalized to other MRAs
- List price of finerenone is $659.10/month

Approach to Medical Therapy for HFpEF

- Titrate **diuretics** to euvolemia
- If no contraindications, add **SGLT2 inhibitor**
- For patients with a BMI≥30, start a **GLP-1 receptor agonist**
- If persistent HF symptoms, start **MRA**

Contraindications and precautions for SGLT2 inhibitors and GLP-1 receptor agonists (semaglutide, tirzepatide)

SGLT2 inhibitors

- Contraindications:
  - Type I DM
  - Type II DM with risk factors for ketoacidosis
- Cautions:
  - Frequent genitourinary infections
  - Volume depletion or hypotension
  - eGFR <20 mL/min per 1.73 m^2 or deteriorating kidney function
  - History or risk of foot amputation

GLP-1 receptor agonists (semaglutide, tirzepatide)

- Contraindications:
  - History of pancreatitis
  - Type I DM
  - Pregnancy
- Cautions:
  - Delayed gastric emptying
  - Thyroid cancer or multiple endocrine neoplasia syndrome 2A or 2B

MRAs

- Contraindications/cautions:
  - Potassium >4.7 mEq/L
  - eGFR <30 mL/min per 1.73 m^2
  - Monitoring for hyperkalemia is not feasible

Bibliography

1. Solomon SD, McMurray JJV, et al. Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction. *NEJM*. 2024; 391:1475-1485. DOI: 10.1056/NEJMoa2407107
2. The BALANCE Investigators. Antibiotic Treatment for 7 versus 14 Days in Patients with Bloodstream Infections. *NEJM*. 2025; 392:1065-1078. DOI 10.10156/NEJMoa2404991
3. Kosiborod MN, Abildstrom SZ, et al. Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity. *NEJM*. 2023;389:1069-1084. DOI: 10.1056/NEJMoa2306963
4. Kosiborod MN, Petrie Mark, et al. Semaglutide in Patients with Obesity-Related Heart Failure and Type 2 Diabetes. *NEJM*. 2024; 390:1394-1407. DOI: 10.1056/NEJMoa2313917
5. Cannata A, McDonagh T. Heart Failure with Preserved Ejection Fraction. *NEJM*. 2025;392:173-184. DOI: 10.1056/NEJMcp2305181
6. Borlaug BA, Colucci WS. 2025. Treatment and Prognosis of Heart Failure with Preserved Ejection Fraction. *UpToDate*. Wolters Kluwer (accessed 09/06/2025). https://www.uptodate.com/contents/treatment-and-prognosis-of-heart-failure-with-preserved-ejection-fraction?search=chronic%20diastolic%20heart%20failure&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1