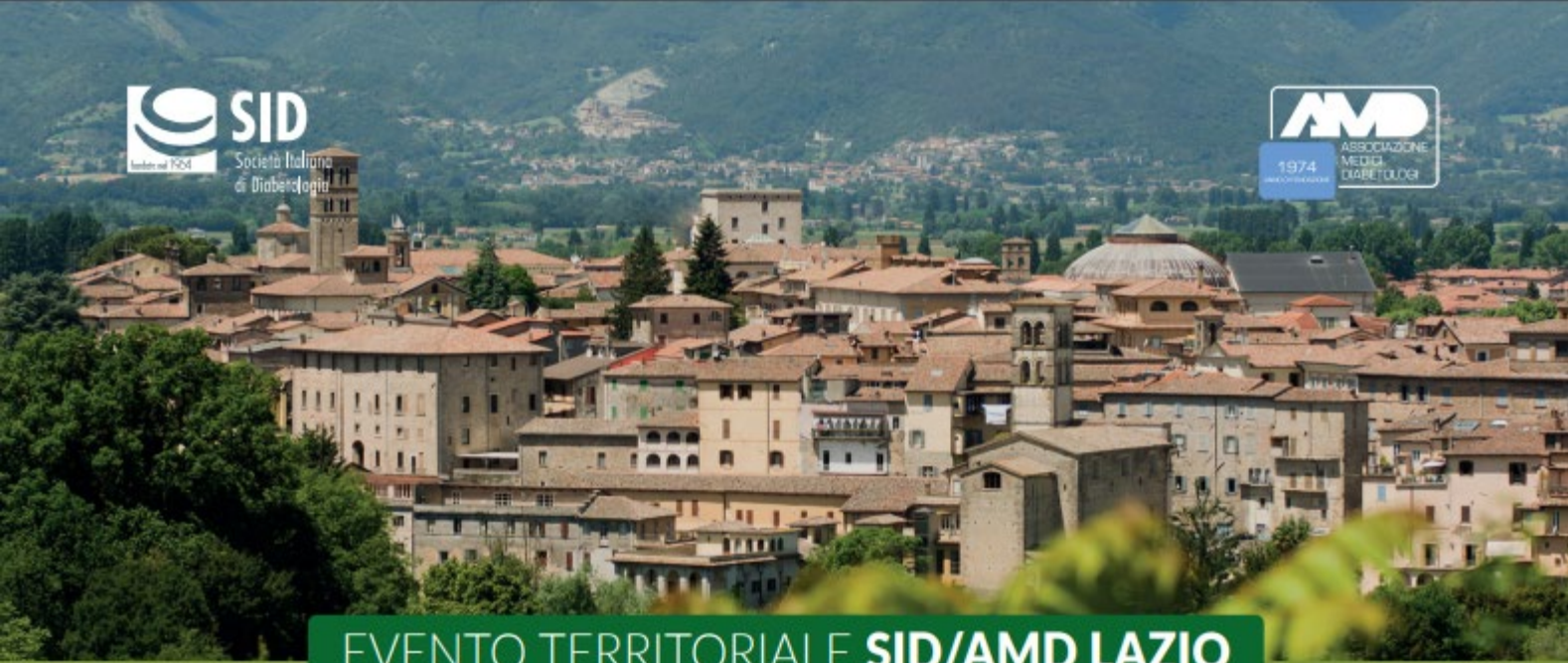


SGLT2i: IL PUNTO DI VISTA DEL CARDIOLOGO



SID
Società Italiana
di Diabetologia

AMD
ASSOCIAZIONE
MEDICI
DIABETOLOGI
1974

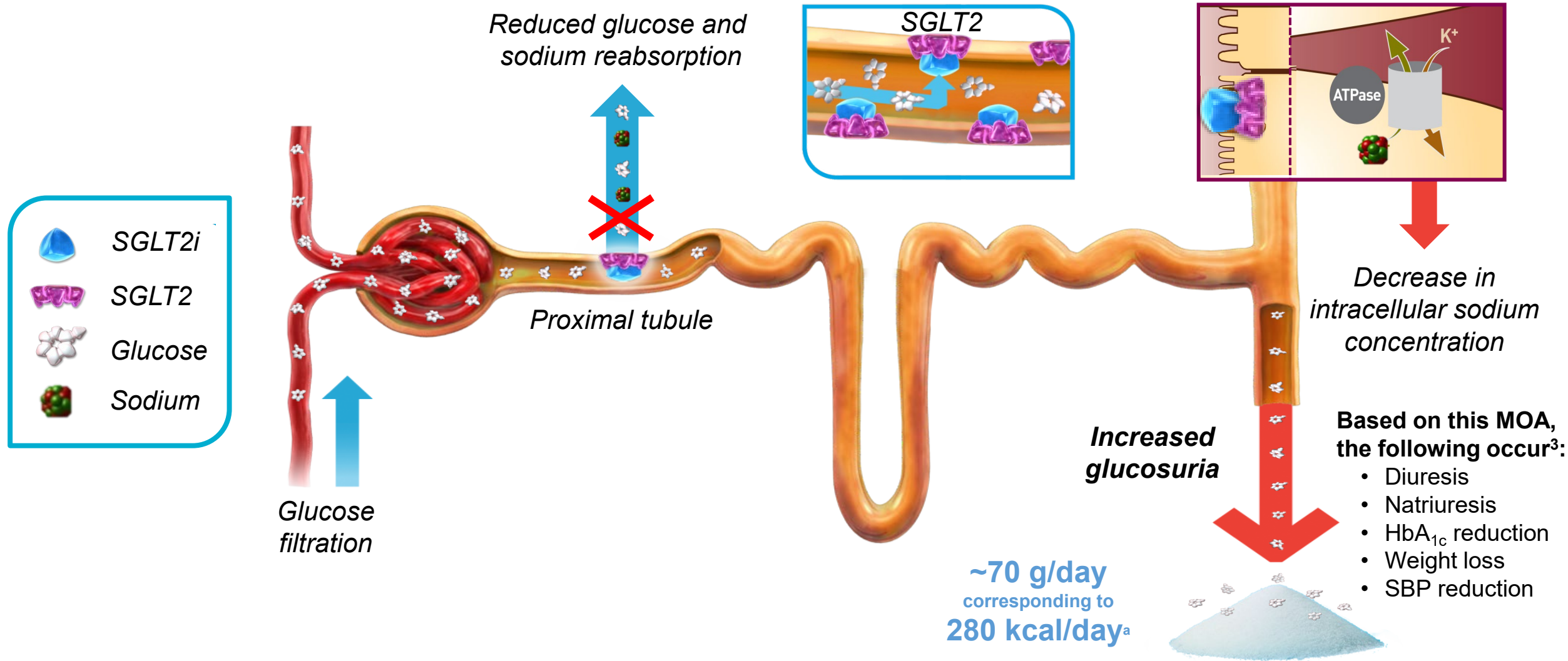
EVENTO TERRITORIALE SID/AMD LAZIO

Protezione cardio-renale nel Diabete di Tipo 2:
L'integrazione tra **Medici di Medicina generale**
e **Specialisti nella cura del Diabete**

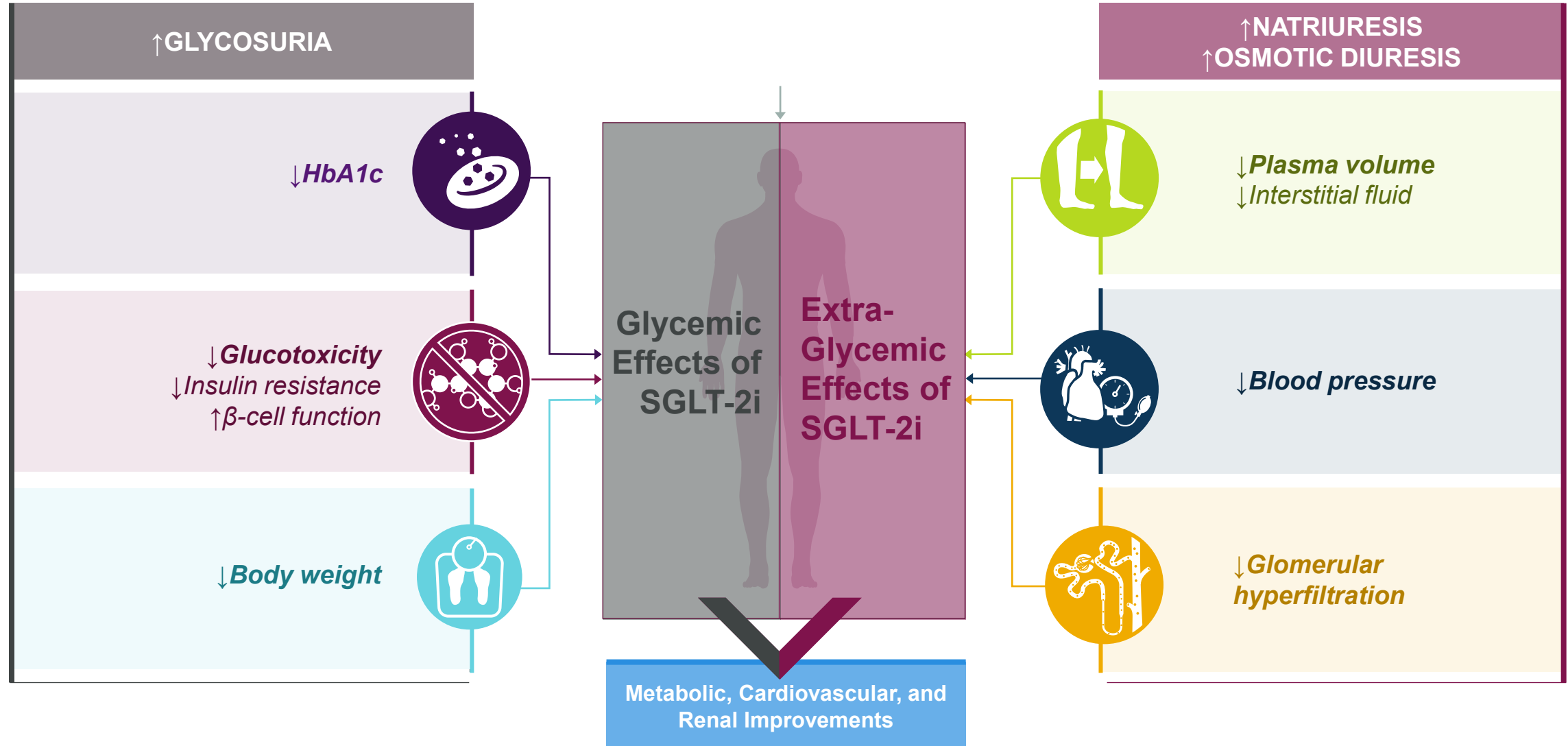
RIETI 17 GIUGNO 2023

Dott.ssa Tania Dominici
Dirigente medico «Ospedale San Camillo de Lellis» ASL RIETI

SGLT2 inhibition: An insulin-independent approach to remove excess glucose by reducing the renal threshold^{1–3}



Key Physiological Effects of SGLT-2 Inhibition

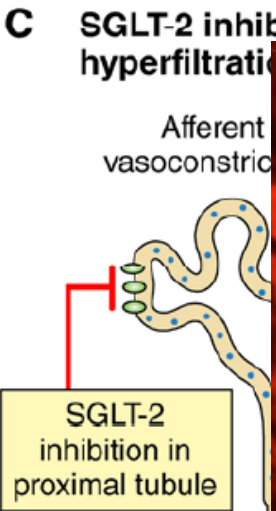
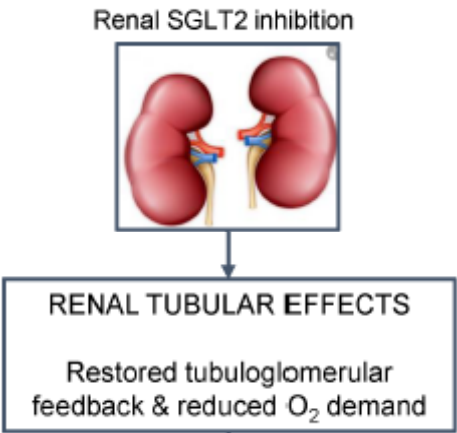


HbA1C=hemoglobin A1C; SGLT-2=sodium-glucose co-transporter 2; SGLT-2i=sodium-glucose co-transporter 2 inhibitor.

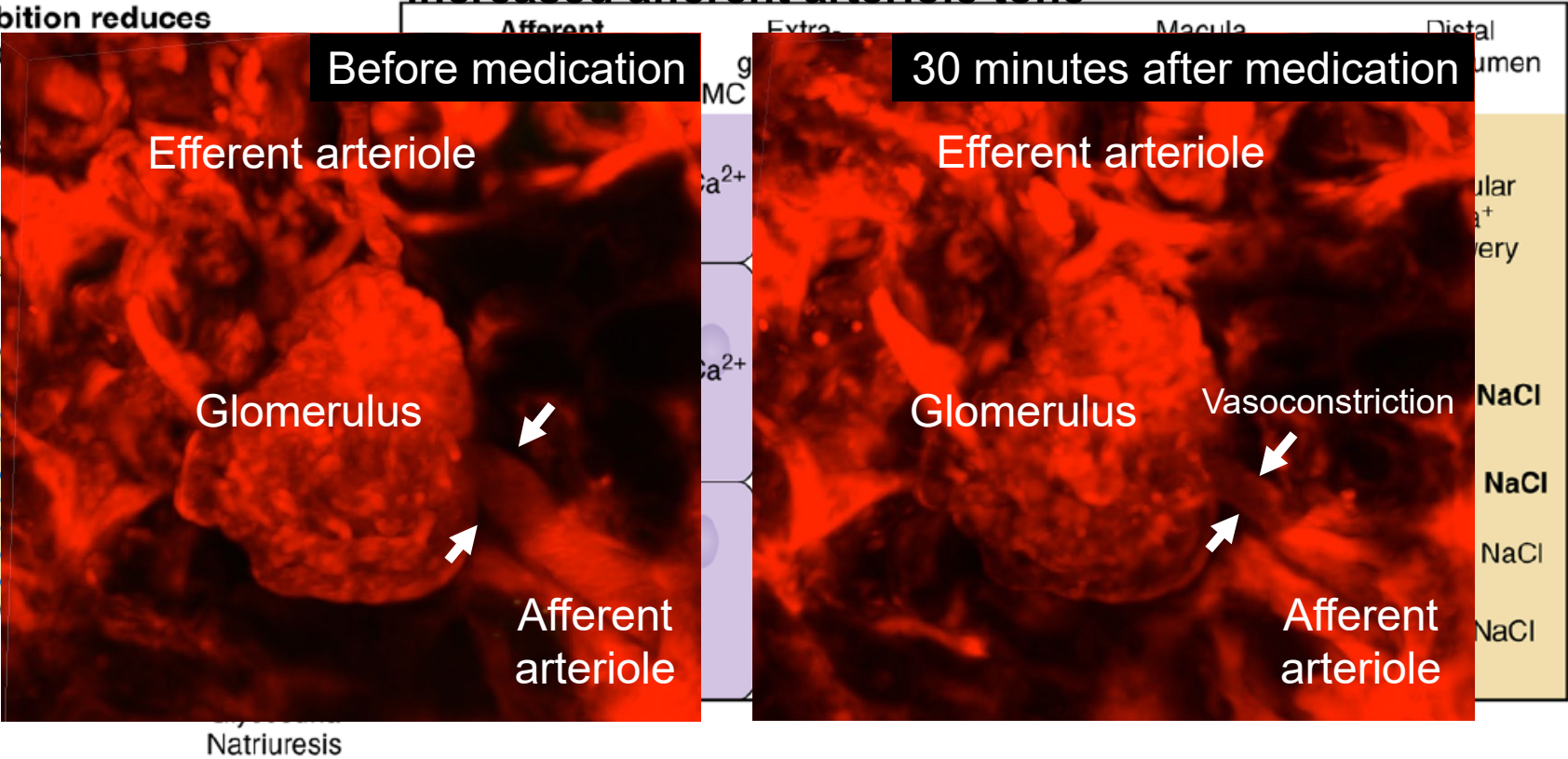
1. Heerspink HJL, et al. *Kidney Int.* 2018;94(1):26-39. 2. van Baar MJB, et al. *Diabetes Care.* 2018;41(8):1543-1556. 3. Tamargo J. *Eur Cardiol.* 2019;14(1):23-32.

Effects of SGLT2 inhibition on cardiorenal pathophysiology

1) RENAL TUBULAR EFFECTS



In vivo imaging showed that SGLT2i therapy increased afferent arteriole tone

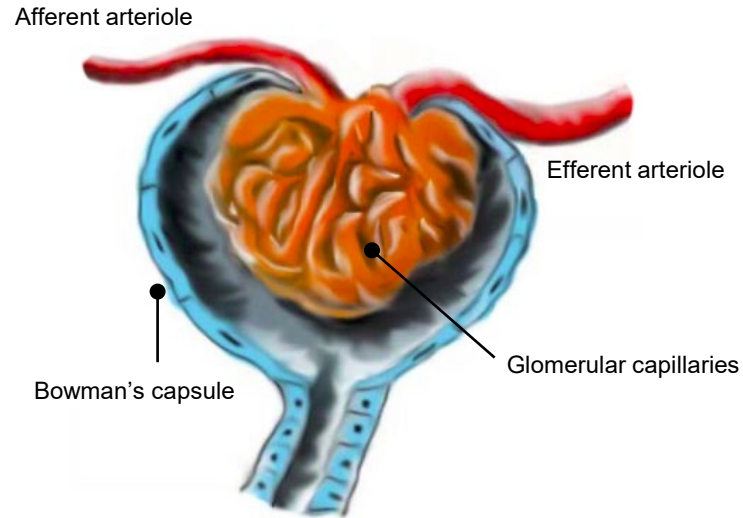


SGLT2 inhibition and RAAS blockade both reduce glomerular hyperfiltration by complimentary mechanisms¹⁻³

SGLT2 inhibitors

Afferent constriction¹⁻³

Due to increased Na⁺ delivery to the macula densa¹⁻³

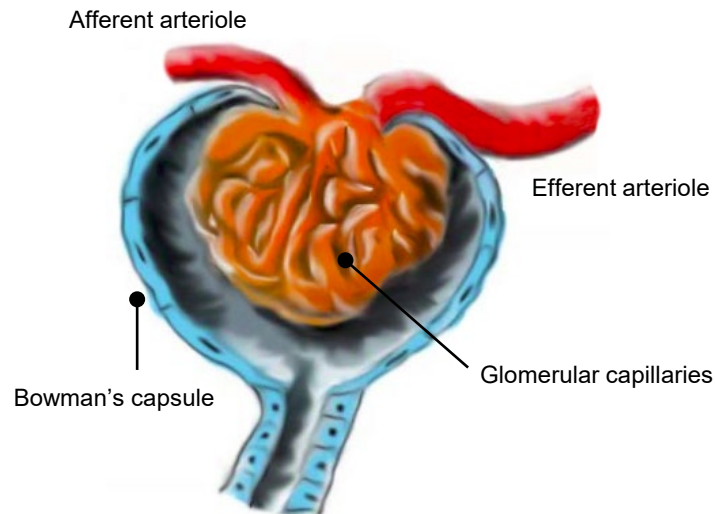


CLINICAL IMPLICATIONS

- Decreased glomerular pressure^{1,3}
- Reduction in albuminuria^{1,2}

RAAS blockade

Efferent vasodilation¹



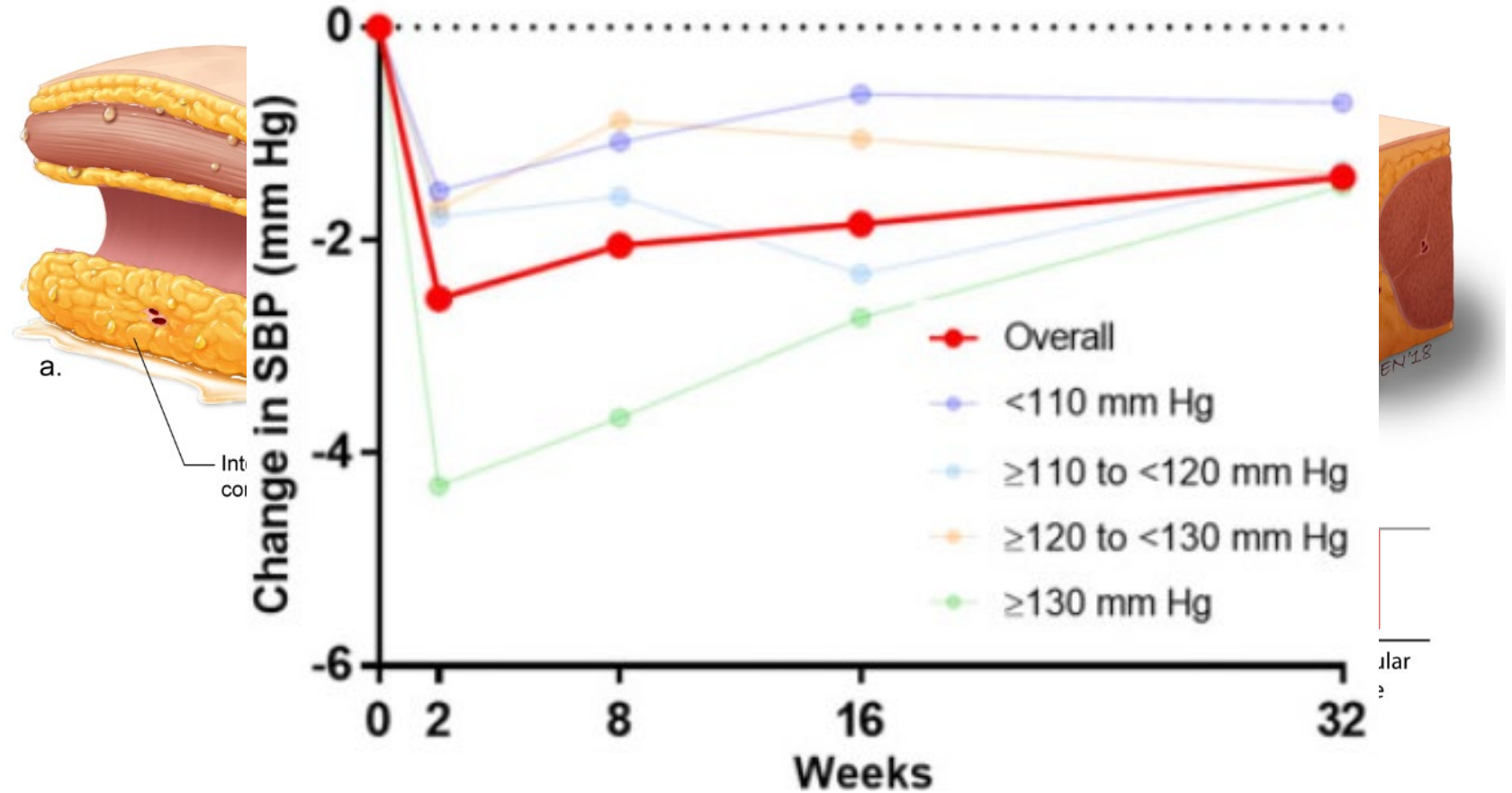
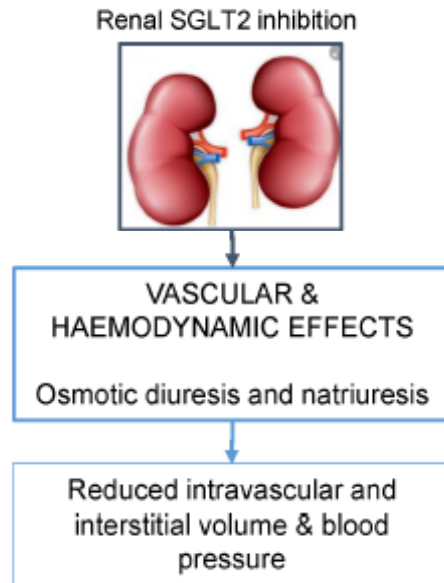
- Decreased glomerular pressure^{1,3}
- Reduction in albuminuria⁴

SGLT2, sodium-glucose cotransporter 2; Na, sodium; RAAS, renin-angiotensin-aldosterone system.

1. Van Bommel EJ, et al. *Clin J Am Soc Nephrol*. 2017;12(4):700-710. 2. Seidu S, et al. *Prim Care Diabetes*. 2018;12(3):265-283. 3. Cherney DZ, et al. *Circulation*. 2014 Feb 4;129(5):587-97. 4. Heerspink HJ, et al. *Diabetes Care*. 2011;34 Suppl 2:S325-9. 5. Adapted from: Shiraishi M, et al. *FASEB J*. 2003;17(15):2284-6.

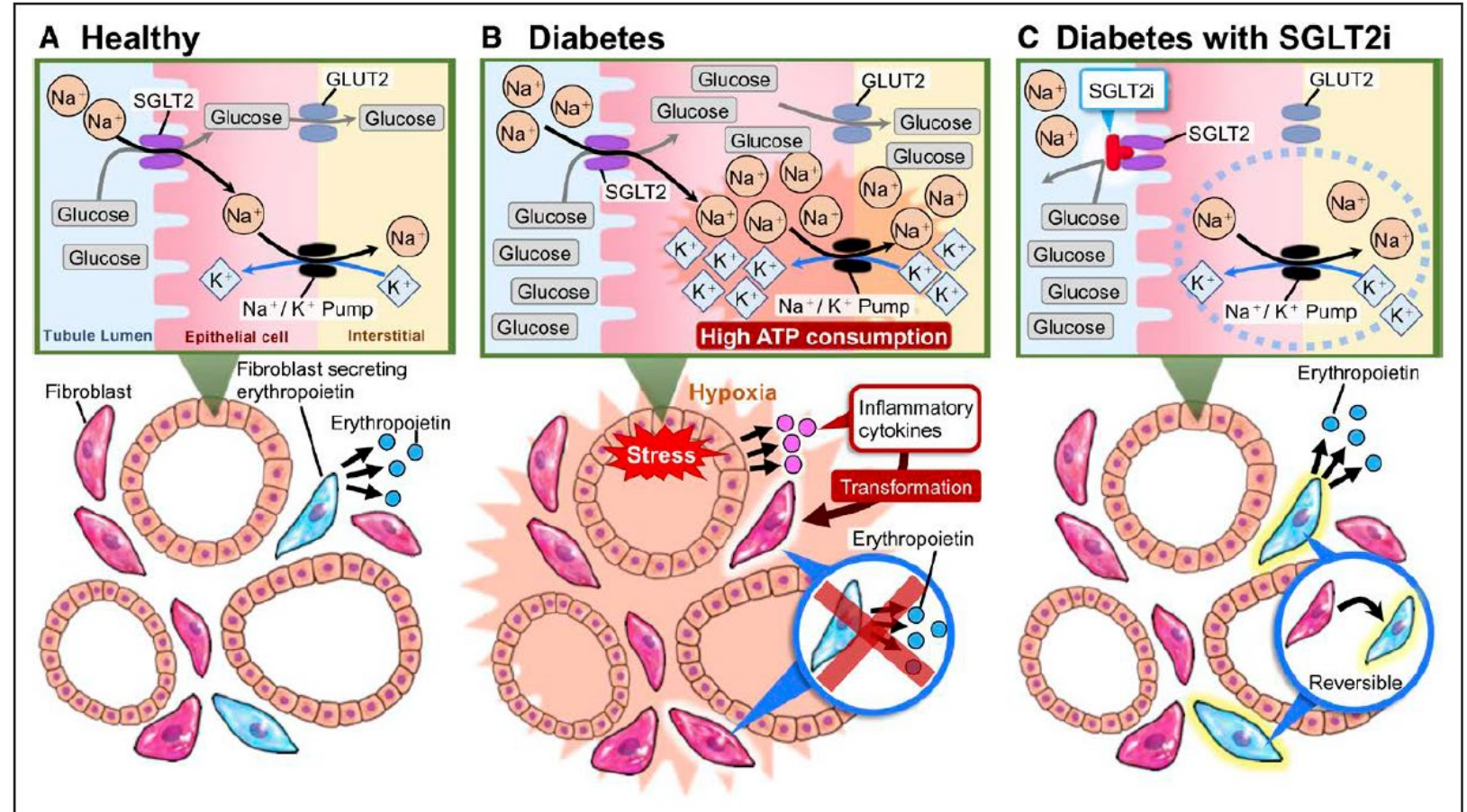
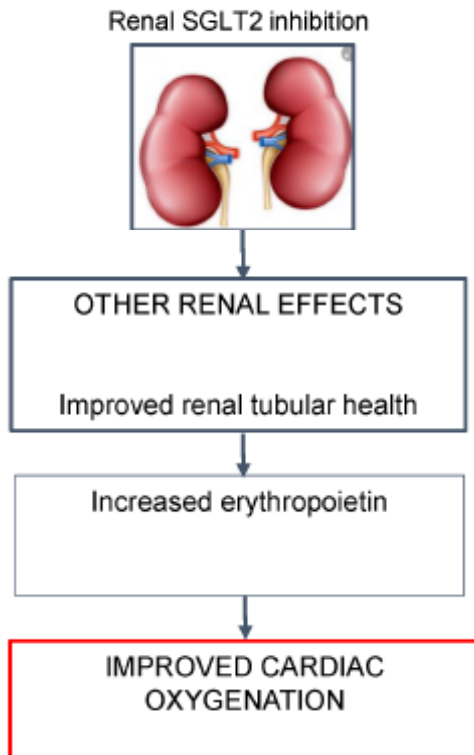
Effects of SGLT2 inhibition on cardiorenal pathophysiology

2) VASCULAR & HAEMODYNAMIC EFFECTS



Effects of SGLT2 inhibition on cardiorenal pathophysiology

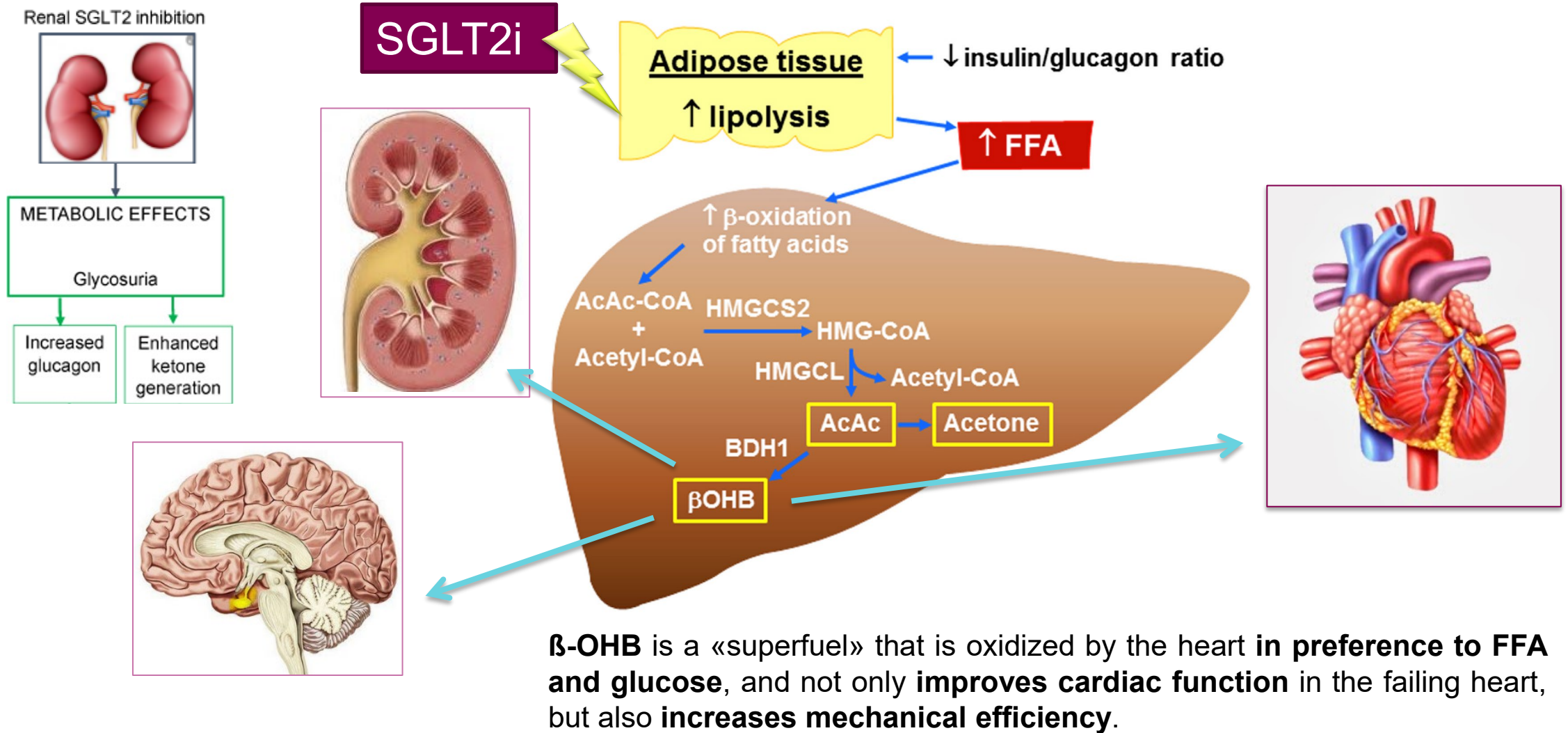
3) OTHER RENAL EFFECTS



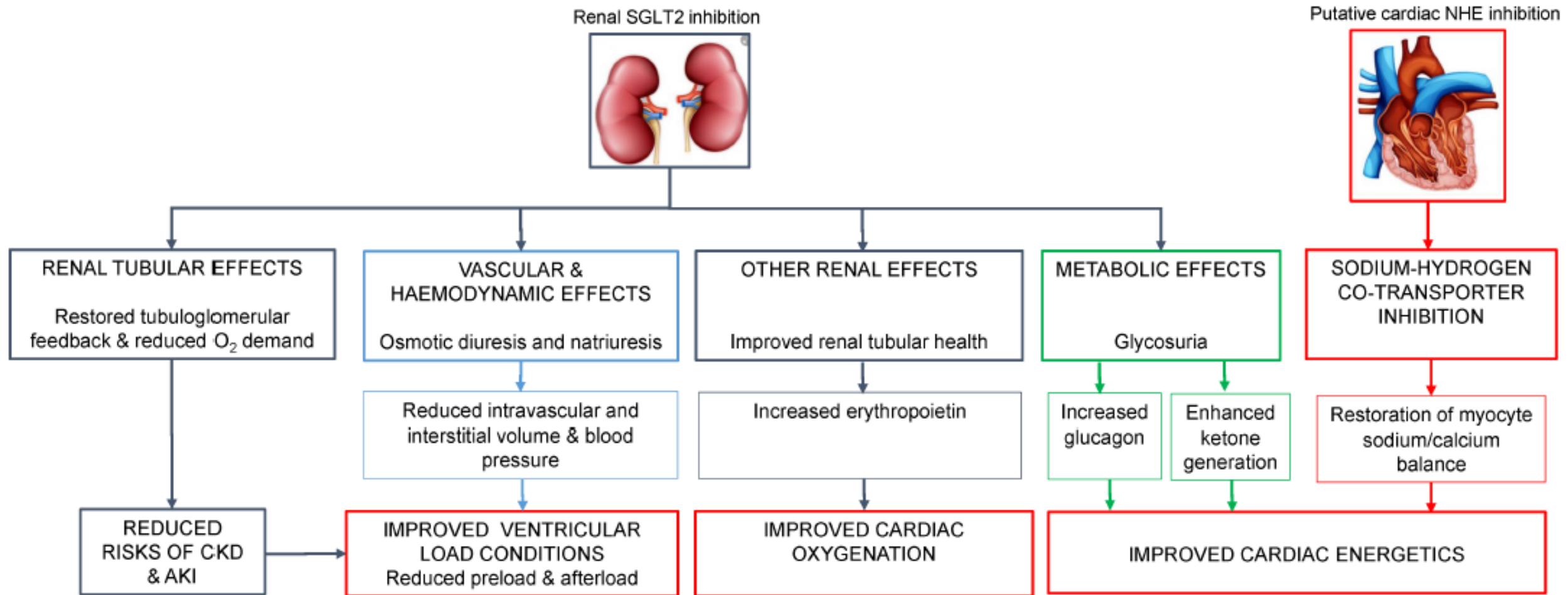
1. ↑ HIF-1 → ↑ Erythropoietin
2. Reduced inflammatory cytokines
3. Reduced ATP consumption

Effects of SGLT2 inhibition on cardiorenal pathophysiology

4) METABOLIC EFFECTS



Effects of SGLT2 inhibition on cardiorenal pathophysiology



What Is Heart Failure?

Proposed Universal Definition of HF¹



Clinical syndrome with symptoms and/or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion.

HF Categories According to LVEF

ESC²

HFrEF	HFmrEF	HFpEF
HF with reduced EF LVEF $\leq 40\%$	HF with mildly reduced EF LVEF 41-49%	HF with preserved EF LVEF $\geq 50\%$

AHA/ACC/HFSA³

HFrEF	HFmrEF	HFpEF	HFimpEF
HF with reduced EF LVEF $\leq 40\%$	HF with mildly reduced EF LVEF 41-49%	HF with preserved EF LVEF $\geq 50\%$	HF with improved EF Previous LVEF $\leq 40\%$ and follow-up LVEF $>40\%$

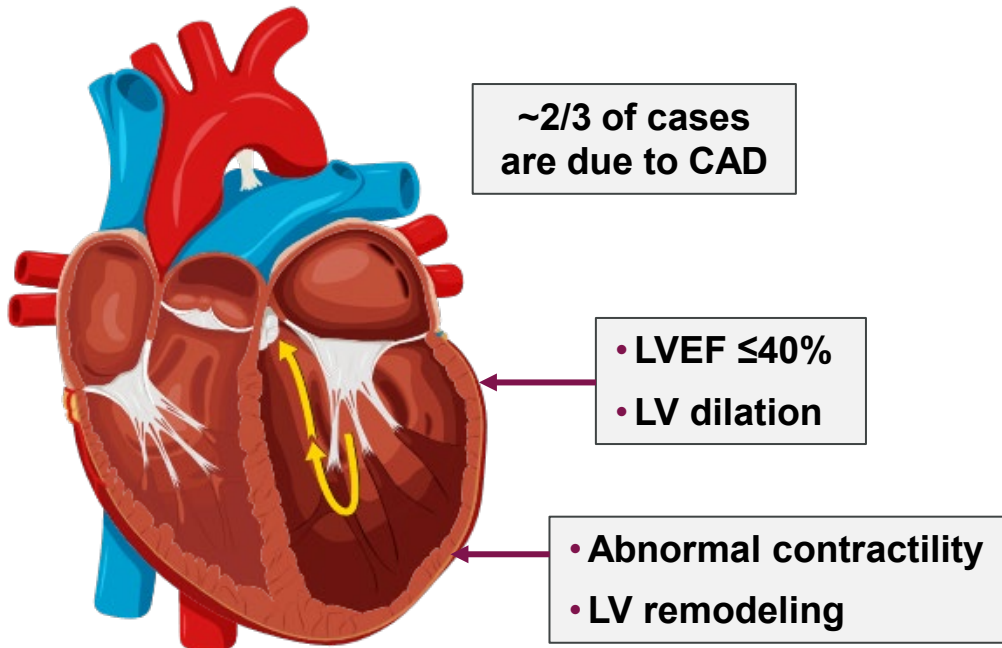
ACC = American College of Cardiology; AHA = American Heart Association; EF = ejection fraction; ESC = European Society of Cardiology; HF = heart failure; HFimpEF = heart failure with improved ejection fraction; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; HFSA = Heart Failure Society of America; LVEF = left ventricular ejection fraction.

1. Bozkurt B et al. *Eur J Heart Fail.* 2021;23(3):352-380; 2. McDonagh TA et al. *Eur Heart J.* 2021;42(36):3599-3726; 3. Heidenreich PA et al. *J Am Coll Cardiol.* 2022;79(17):e263-e421.

Differences in HF Pathophysiology¹⁻³

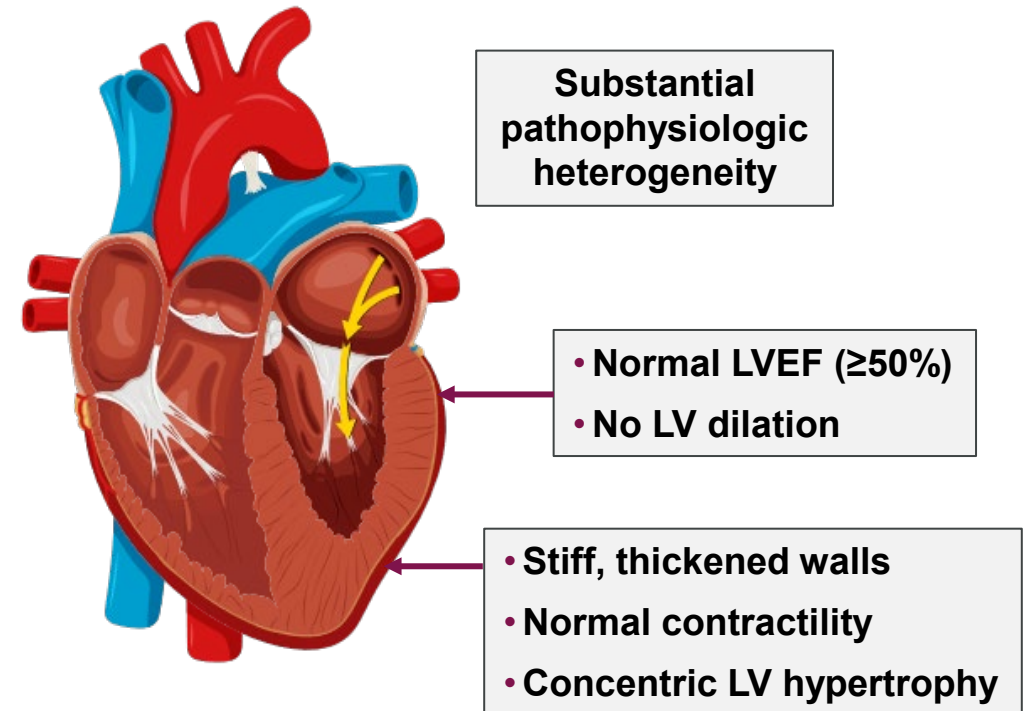
HFrEF

LV contraction is reduced resulting in inadequate cardiac output.



HFpEF

LV filling is reduced so that, even though LVEF is normal, cardiac output is reduced.



CAD = coronary artery disease; HF = heart failure; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; HTN = hypertension; LV = left ventricular; LVEF = left ventricular ejection fraction.

1. Bloom MW et al. *Nat Rev Dis Primers*. 2017;3:17058; 2. Borlaug BA. *Nat Rev Cardiol*. 2014;11:507-515; 3. Redfield MM. *N Engl J Med*. 2016;375:1868-1877.

HF is a growing public health problem, with high morbidity and mortality

BURDEN

HF affects
~64 million
people
worldwide¹



Over 50% of patients
with HF have **HFpEF**²

HOSPITALIZATION



HF is the **number one cause of hospitalization**
in people >65 years^{2,a}



hHF is **projected to rise by ~50%** over
the next 25 years³

MORTALITY



The 5-year mortality
rate for patients with
HF is **~50%**⁴

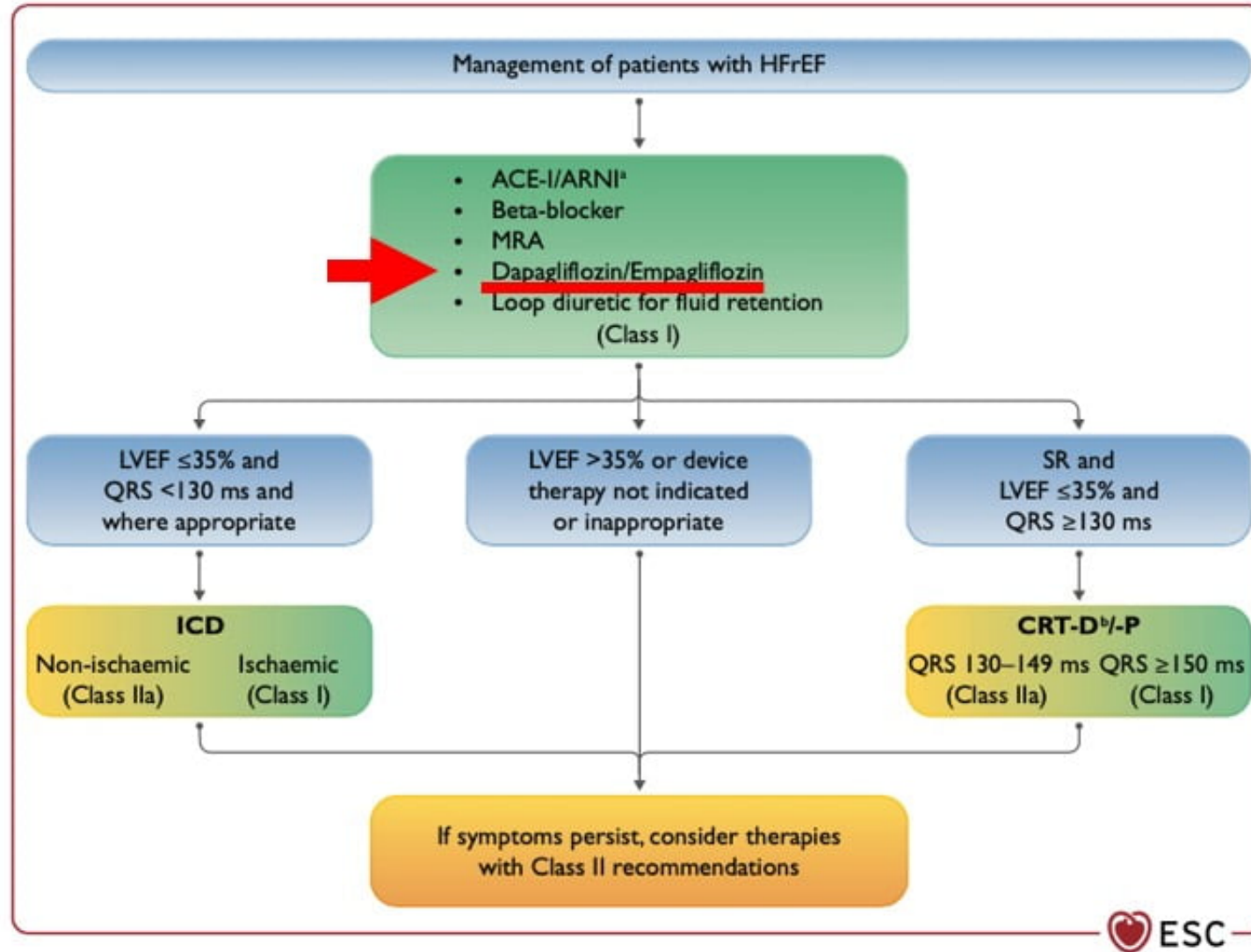


Mortality significantly increases after each
HF readmission⁵

^aIn developed countries.

1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Lancet. 2018;392(10159):1789-1858; 2. Cowie MR et al. ESC Heart Fail. 2014;1(2):110-145; 3. Groenewegen A et al. Eur J Heart Fail. 2020;22(8):1342-1356; 55; 4. Jones NR et al. Eur J Heart Fail. 2019;21(11):1306-1325; 5. Setoguchi S et al. Am Heart J. 2007;154(2):260-266;

ESC 2021 Guidelines HFrEF



ESC 2021 Heart Failure Guidelines: Dapagliflozin is Recommended in Patients with HFrEF to Reduce the Risk of HF Hospitalization and Mortality

Recommendations	Class ^a	Level ^b
An ACEI is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
Sacubitril/valsartan is recommended as a replacement for an ACEI in patients with HFrEF to reduce the risk of HF hospitalization and death.	I	B

^aClass of recommendation; ^bLevel of evidence.

ACEI = angiotensin-converting enzyme inhibitor; ESC = European Society of Cardiology; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist.

McDonagh TA et al. Online ahead of print. *Eur Heart J*. 2021.

I pilastri della terapia HFrEF 2021



ACE i/ARB

**Neprilysin
inhibitor**

Beta-blocker

MRA

**SGLT2
inhibitor**



ESC

European Society
of Cardiology

European Heart Journal (2021) 42, 681–683
doi:10.1093/eurheartj/ehaa1012

EDITORIAL

Heart failure drug treatment: the fantastic four

Johann Bauersachs *

Department of Cardiology and Angiology, Hannover Medical School, Hannover, Germany

Online publish-ahead-of-print 11 January 2021

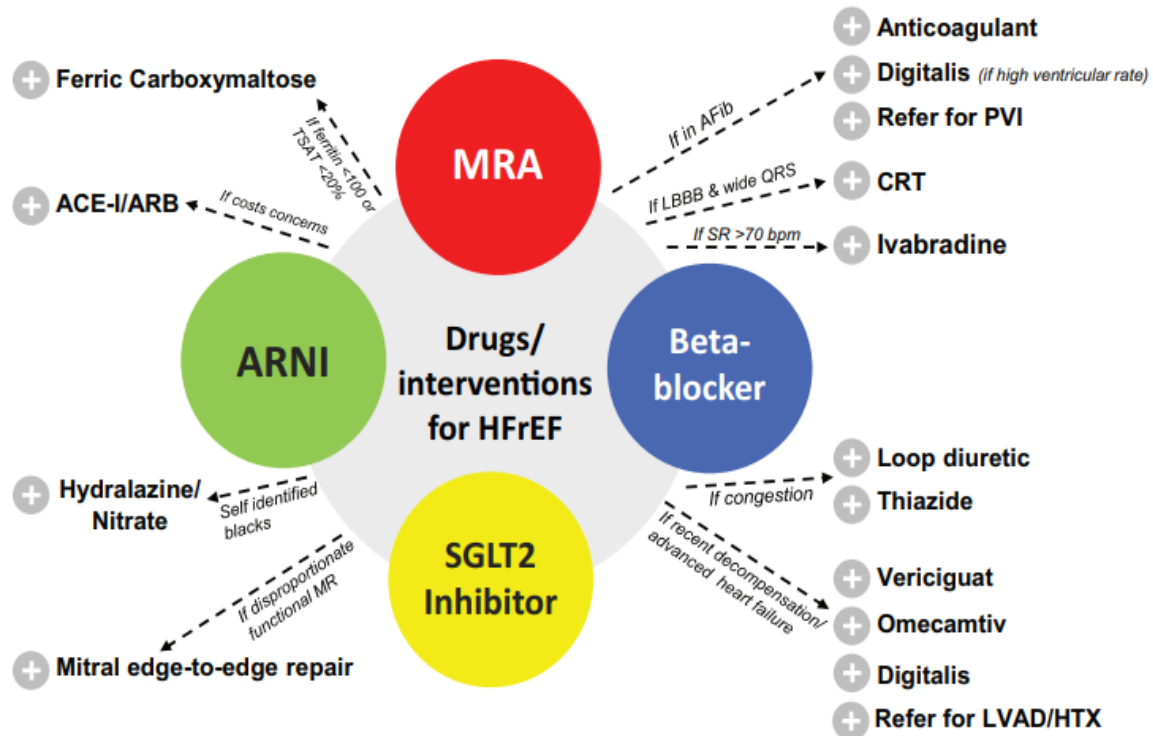


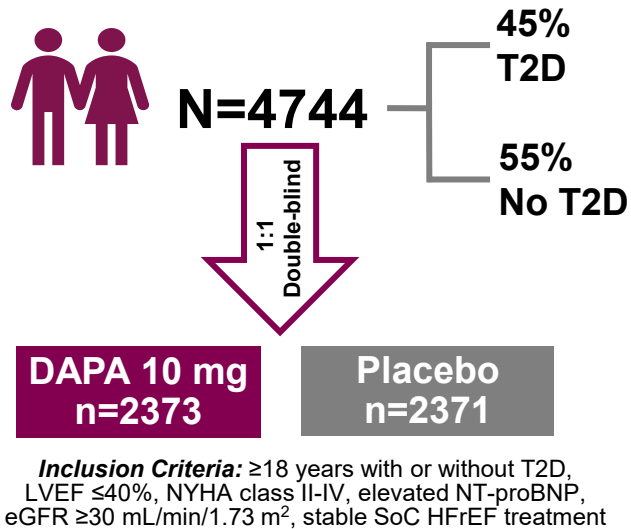
Figure 1 Drug, interventional, and device treatment for heart failure with reduced ejection fraction (HFrEF). ACE-I, angiotensin-converting enzyme inhibitor; Afib, atrial fibrillation; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor/neprilysin inhibitor; CRT, cardiac resynchronization therapy; HTX, heart transplantation; LBBB, left bundle branch block; LVAD, left ventricular assist device; MR, mitral regurgitation; MRA, mineralocorticoid receptor antagonist; PVI, pulmonary vein isolation; SGLT2, sodium–glucose co-transporter 2; SR, sinus rhythm; TSAT, transferrin saturation.

In clinical practice, patients without contraindications appear to **gain most benefit from combined treatment with the ‘fantastic four’**: an ARNI, a beta-blocker, an MRA, and an SGLT2 inhibitor.

DAPA-HF

First and Largest SGLT2i HFrEF Trial
to Successfully Improve Outcomes and Symptoms^{2,5}

DAPA-HF Overview⁵



Significant Reduction in Composite of CV Death or Worsening HF^{5,b}

26% RRR
HR 0.74 (0.65-0.85)
p<0.001

NNT=21

CV Death⁶

18% RRR
p=0.029

hHF⁶

30% RRR
p=0.00003
[Includes urgent HF visits]

Consistent Benefit Across a Broad and Representative Population

T2D/No T2D⁷ Baseline LVEF¹⁰
Background HF therapy⁸ NT-proBNP¹¹
Diuretic use and dose⁹ eGFR¹²

↓ Risk of both **first and recurrent hHF events**¹³

↓ Reduction in **all-cause mortality** (p=0.022^c)⁶

✓ **HF symptom improvement**
more common and deterioration less common¹⁴

Significantly reduced risk
of CV death or worsening HF^b **as early as**¹⁵



DAPA-HF Safety^{5,7}

DAPA was well-tolerated in patients with and without T2D

Adverse events rarely led to discontinuation of treatment
No events of major hypoglycemia or DKA in patients without T2D

Overview of results from EMPEROR-Reduced¹

Primary outcome

**HHF or
CV death**



↓ **25% RRR**
 $p < 0.001$

Secondary outcomes

Total HHF*



↓ **30% RRR**
 $p < 0.001$

eGFR slope[†]



**+1.73
difference**
 $p < 0.001$

Exploratory outcomes

**Composite
kidney
outcome[‡]**



HR 0.50
(95% CI 0.32, 0.77)
NA

**KCCQ clinical
summary
score**



1.75 rate ratio
 $p = 0.0058$

The rates of AEs were similar between empagliflozin and placebo¹

SGLT2i Early Use



ESC

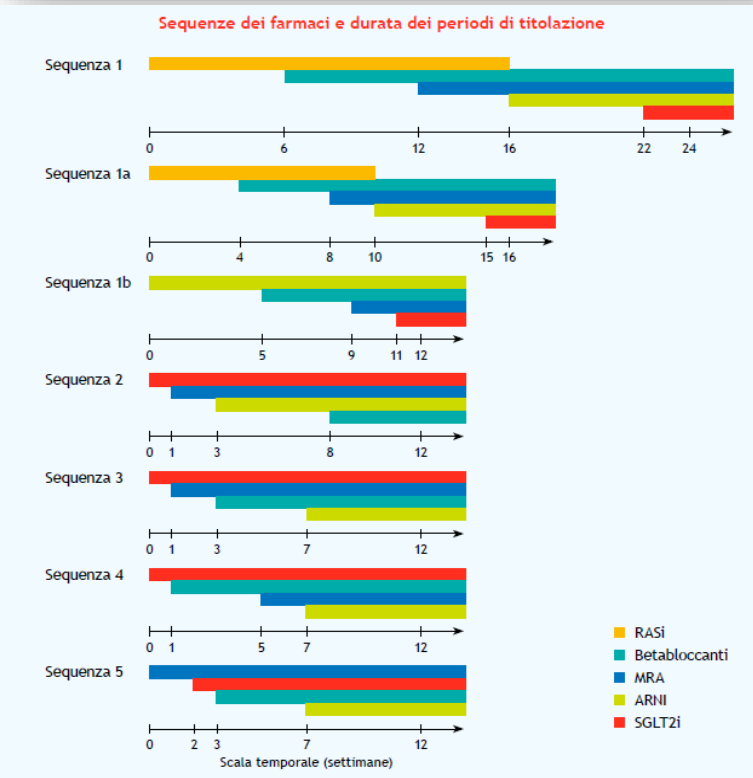
European Heart Journal (2022) 43, 2573–2587
https://doi.org/10.1093/eurheartj/ehac210

CLINICAL RESEARCH

Heart failure and cardiomyopathies

Accelerated and personalized therapy for heart failure with reduced ejection fraction

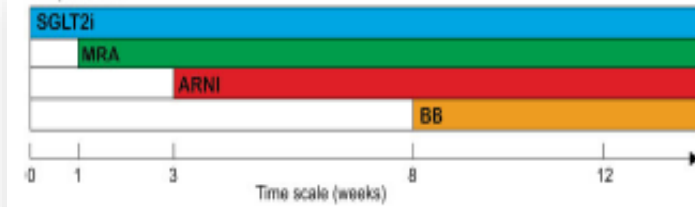
Li Shen^{1,2}, Pardeep Singh Jhund², Kieran Francis Docherty², Muthiah Vaduganathan³, Mark Colquhoun Petrie², Akshay Suvas Desai³, Lars Køber⁴, Morten Schou⁵, Milton Packer^{6,7}, Scott David Solomon³, Xingwei Zhang¹, and John Joseph Valentine McMurray^{2*}



Sequence 1

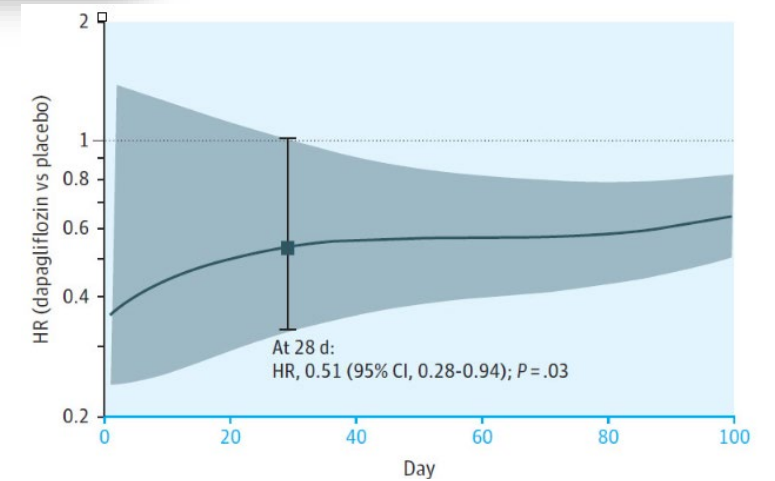


Sequence 2



«When Sequence 2 was compared with the standard approach (Sequence 1), the number of patients who could have avoided an event* was almost doubled, thanks to increased titration rate and drug order modification.

* CV death or hospitalization for HF



SGLT2i Early Use

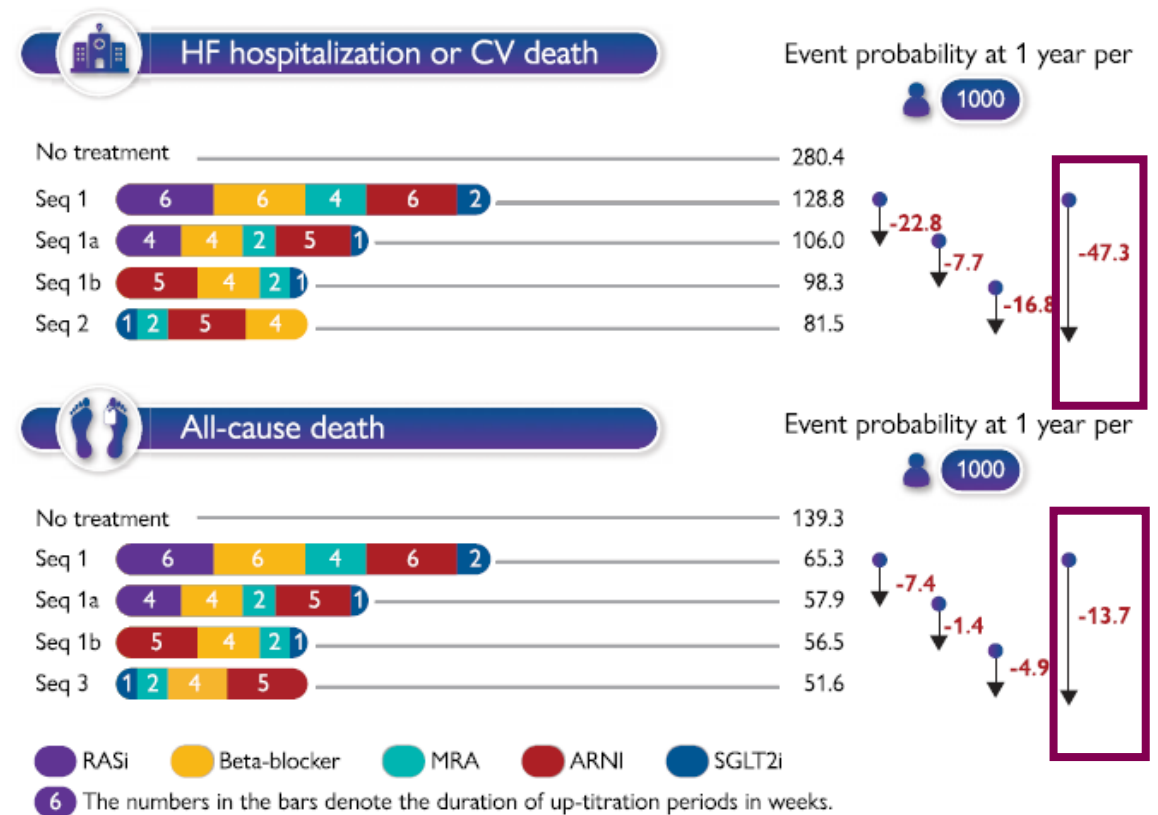


European Heart Journal (2022) 00, 1–15
<https://doi.org/10.1093/eurheartj/ehac210>

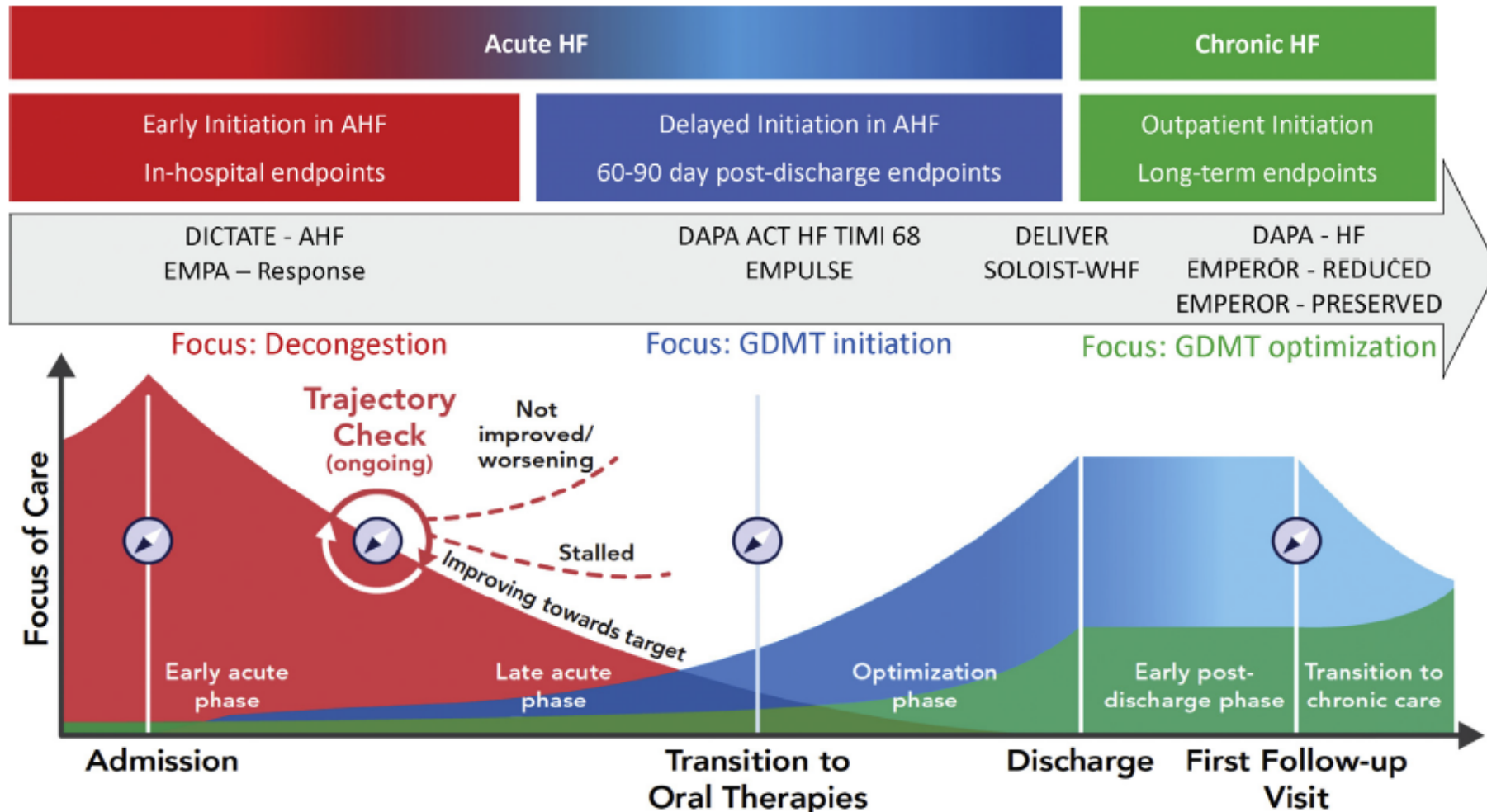
CLINICAL RESEARCH
Heart failure and cardiomyopathies

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Li Shen^{1,2}, Pardeep Singh Jhund², Kieran Francis Docherty²,
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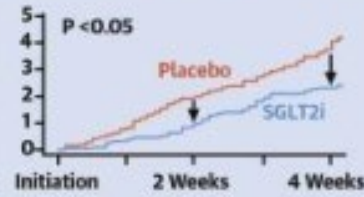
SGLT2i use in acute and chronic HF



In-Hospital Initiation of SGLT2i for HFrEF

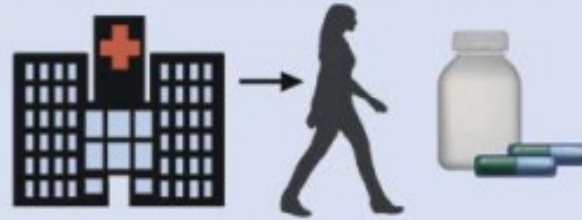
Patients-centered benefits

Early clinical benefit within days to weeks of initiation



Deferring in-hospital initiation exposes patients to excess risk of early post-discharge clinical worsening, readmission, and death.

Deferred in-hospital initiation of GDMT is associated with never initiating



Among patients eligible for therapy, discharging without medication associated with >75% chance will not be started within 1 year.

Potential improved tolerance to other evidence-based therapies



Hospitalized population vulnerable to in-hospital and post-discharge discontinuation of GDMT may particularly benefit from ↓ risk of hyperkalemia and worsening renal function.

Safety and Tolerability

Favorable blood pressure and kidney profile



Minimal to no effect on blood pressure, and no excess risk of symptomatic hypotension. No adverse renal effects (instead preserves kidney function and prevents dialysis).

Favorable glycemic safety profile



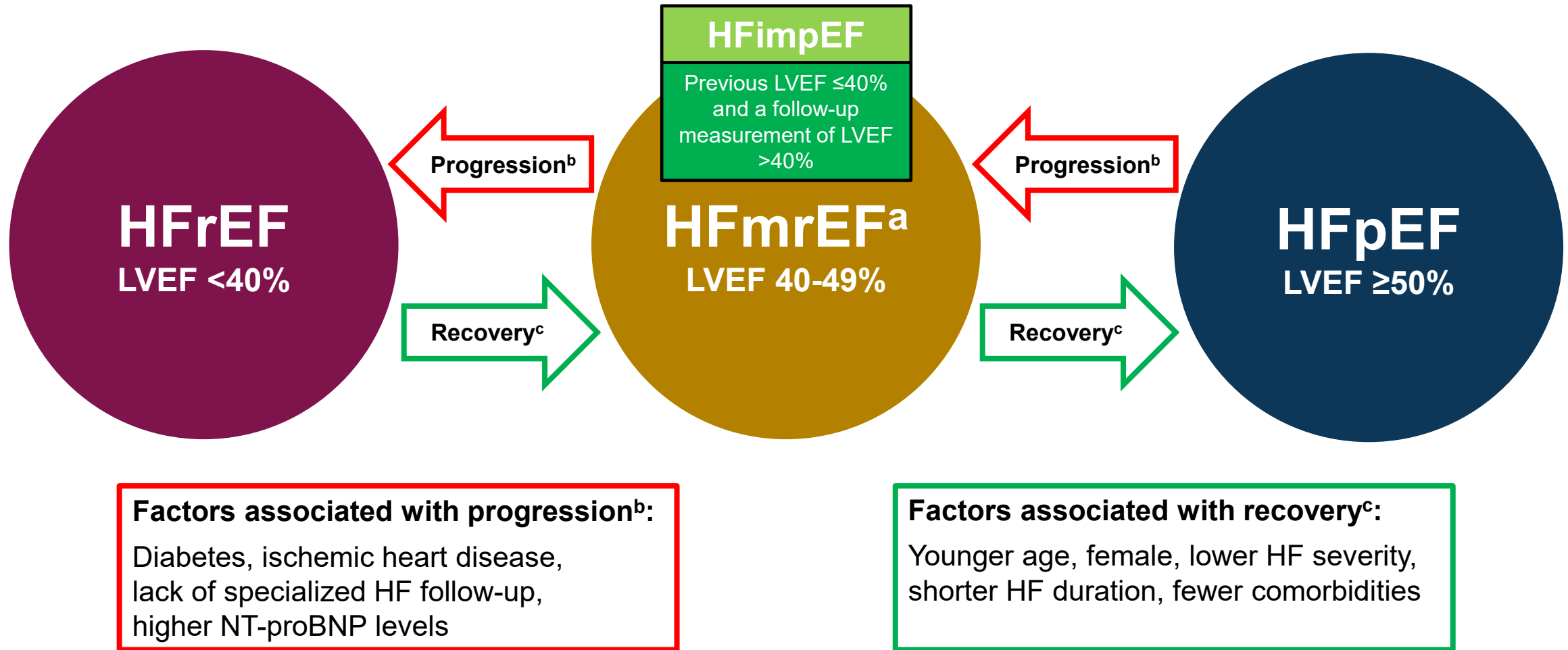
No excess risk of hypoglycemia in clinical trials.
No excess risk of DKA in HFrEF trials
(↑ absolute risk of DKA <0.2% across all SGLT2i trials).

Well-tolerated and safe, including among high-risk subgroups



Numerically fewer serious adverse events than placebo. Rarely symptomatic side effects and well tolerated among older patients.

Changes in LVEF Occur Over Time and Are Associated With Specific Patient Characteristics



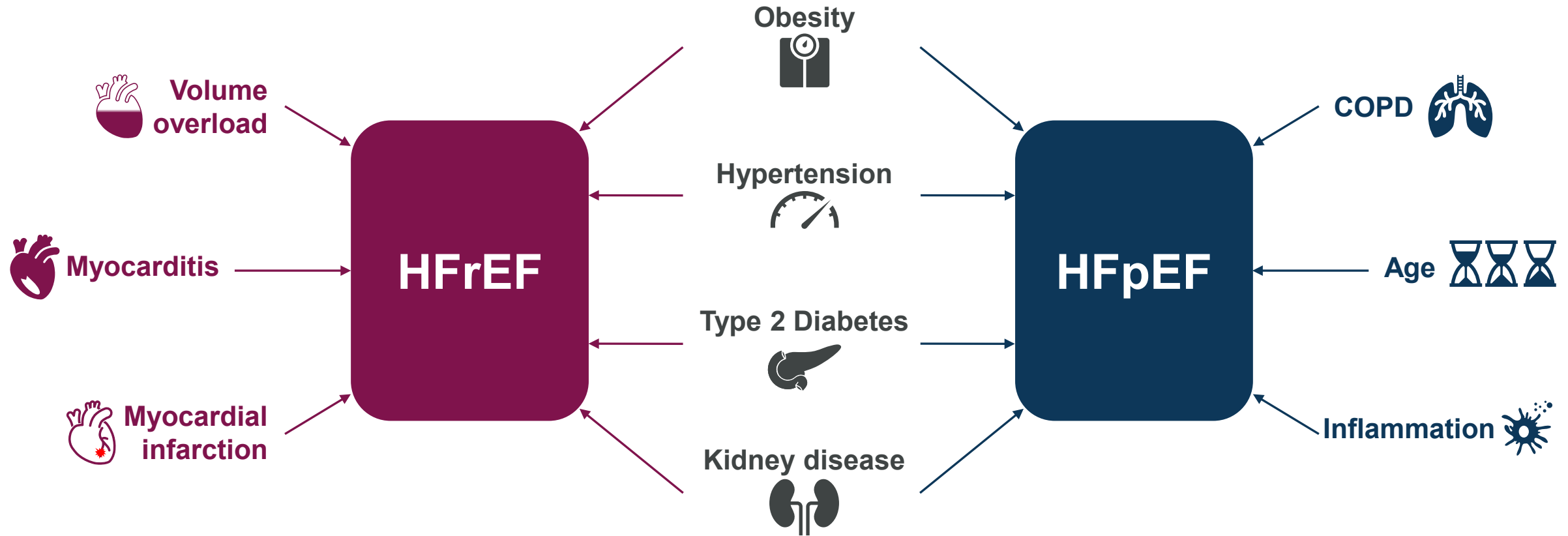
Data from patients with ≥2 EF measurements in the SwedeHF study (N=4942) between May 2000 and December 2012.

^aReference uses the term HF with midrange EF (EF 40-49%) for this group; ^bEF decrease; ^cEF increase.

EF = ejection fraction; HF = heart failure; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide.

Savarese G et al. *JACC Heart Fail.* 2019;7:306-317.

HFrEF and HFpEF Share Many Comorbidities and Risk Factors, While Others Differ



COPD = chronic obstructive pulmonary disease; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction.

Simmonds SJ et al. *Cells*. 2020;9:242.

Recommendations for the treatment of patients with heart failure with preserved ejection fraction

Recommendations	Class	Level
Screening for, and treatment of, aetiologies, and cardiovascular and non-cardiovascular comorbidities is recommended in patients with HFpEF (see relevant sections of this document).	I	C
Diuretics are recommended in congested patients with HFpEF in order to alleviate symptoms and signs.	I	C

HFpEF = heart failure with preserved ejection fraction.

Guidelines Consistently Recommend SGLT2i as Class 1A Therapy for HFrEF^{1,2}

	 ESC European Society of Cardiology	 American Heart Association.  AMERICAN COLLEGE of CARDIOLOGY  HFSA HEART FAILURE SOCIETY OF AMERICA
Class 1A recommendation to reduce hospitalization for HF and mortality ^a	✓	✓
First Line Therapy with ACEI/ARNI ^b , beta-blockers and MRA	✓	✓
Initiate during hospitalization and promptly optimize	✓	✓

2022 AHA/ACC/HFSA Guidelines also **recommend SGLT2i** for the treatment of **HFmrEF and HFpEF**

^aAHA/ACC/HFSA guidelines recommend SGLT2i to reduce the risk of hospitalization for HF and CV mortality; ^bAHA/ACC/HFSA guidelines also recommend ARB to reduce morbidity and mortality in patients with previous or current symptoms of chronic HFrEF who are intolerant to ACEI because of cough or angioedema and when the use of ARNI is not feasible.

ACC = American College of Cardiology; ACEI = angiotensin-converting enzyme inhibitor; AHA = American Heart Association; ARB = angiotensin-receptor blocker; ARNI = angiotensin-receptor neprilysin inhibitor; CV = cardiovascular; ESC = European Society of Cardiology; HF = heart failure; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; HFSA = Heart Failure Society of America; MRA = mineralocorticoid receptor antagonist; SGLT2i = sodium-glucose cotransporter 2 inhibitor.

1. McDonagh TA et al. *Eur Heart J*. 2021;42:3599-3726; 2. Heidenreich PA et al. *J Am Coll Cardiol*. 2022;79(17):e263-e421.

EMPEROR-Preserved: Empagliflozin Outcome Trial in Patients with Chronic Heart failure with Preserved Ejection Fraction

Purpose:

Evaluate the effects of SGLT2 inhibitor (Empagliflozin) on cardiovascular death and heart failure hospitalizations in patients with heart failure with a preserved ejection fraction (HFpEF), with or without diabetes.

Trial Design: N=5998, International multicenter (622 centers in 23 countries) randomized placebo controlled, double-blind, event-driven study. Symptomatic HFpEF patients (LVEF>40%) received empagliflozin (10mg once daily) or placebo, in addition to usual therapy. Median follow up period was 26 months.

Primary Endpoint: Composite of CV death or heart failure hospitalization.

Secondary Endpoints: Heart Failure hospitalizations(including first and recurrent events), rate of decline in eGFR during treatment.

	Empagliflozin n=2997	Placebo n=2991	HR (95% CI)	P-value
Primary Composite Outcome: Composite of CV death or HF hospitalization	415 (13.8%)	511 (17.1%)	0.79 (0.69-0.90)	< 0.001
HF hospitalization	259 (8.6%)	352 (11.8%)	0.71 (0.60-0.83)	
Cardiovascular Death	219 (7.3%)	244 (8.2%)	0.91 (0.76-1.09)	
Secondary Outcomes specified in hierarchical testing procedure				
Total number of HF hospitalizations	407	541	0.73 (0.61-0.88)	< 0.001
eGR mean slope change per year (ml/min/1.73m ²)	-1.25±0.11	-2.62±0.11	1.36 (1.06-1.66)	< 0.0001
Results: Empagliflozin reduced the combined risk of cardiovascular death or heart failure hospitalization in patients with HFpEF by 21%, regardless of the presence or absence of diabetes. This benefit was consistent across pre-specified EF subgroups. Empagliflozin reduced total (first and recurrent) hospitalizations for HF by 27%.				

Results reflect the data available at the time of presentation.



DELIVER: The largest and broadest trial to date in patients with LVEF >40%¹

DELIVER^{1,2} N=6263

- LVEF >40% and evidence of structural heart disease
- Elevated NT-proBNP
- Ambulatory or hospitalized
- eGFR ≥25 mL/min/1.73 m²

1:1 randomization

DAPA 10 mg

Placebo

Median follow-up: 2.3 years

Primary endpoint²



Composite of CV death or worsening HF (hHF or an urgent HF visit):

- Full patient population
- Patients with LVEF <60%

Secondary endpoints²

- Total number of hHF (first and recurrent) and CV death
- Change in KCCQ-TSS from baseline to 32 weeks
- CV death
- All-cause mortality

Baseline characteristics^{1,2}



72 years
Mean Age



75%
NYHA class II



1011 pg/mL
Median NT-proBNP



54%
Average LVEF



55%
Without T2D



50%
With an eGFR <60 mL/min/1.73 m²

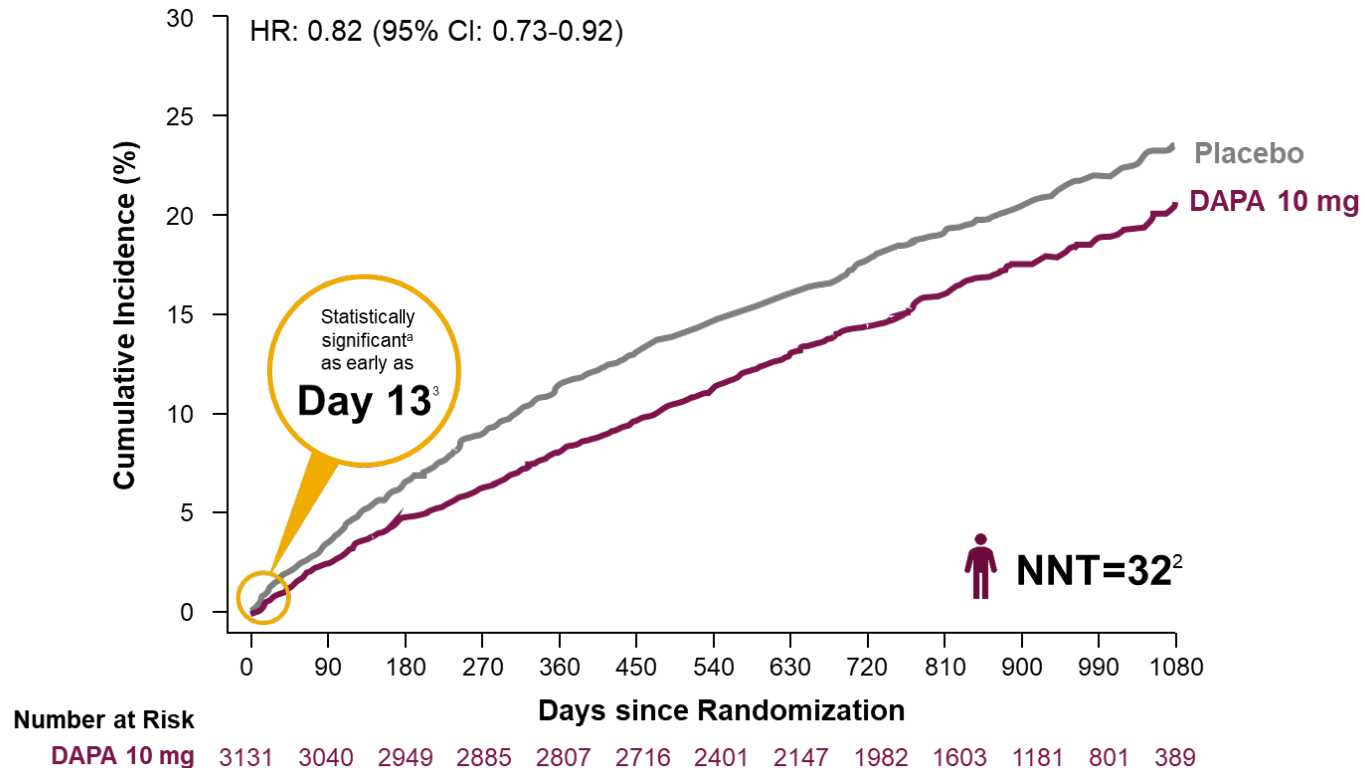


16%
Hospitalized or discharged <90 days



~18%
With prior LVEF ≤40%

DELIVER: Dapagliflozin significantly reduced the risk of CV death and worsening HF^a in patients with HFmrEF and HFpEF¹



CV Death or Worsening HF^a

18%
RRR

3.1% ARR
p=0.0008

CV death

12%
RRR

1% ARR
0.88 (0.74, 1.05)

Worsening HF^a

21%
RRR

3.7% ARR
0.79 (0.69, 0.91)

Consistent benefit in the primary endpoint across key subgroups

All-cause mortality was also reduced in the dapagliflozin group

All-cause mortality
6%
RRR

~1% ARR
0.94 (0.83, 1.07)

Quality of life

2.4 Points
TSS-KCCQ

P<0.001

^aNominal significance at Day 13 (HR, 0.45; 95% CI, 0.20-0.99; p=0.046), with sustained statistical significance starting at Day 15.

1. Solomon SD et al. *N Engl J Med*. 2022;387(12):1089-1098

Major guidelines recommend SGLT2 inhibitors across HFrEF, HFmrEF, and HFpEF to reduce hHF and CV mortality^{1,2}



HF type	COR	LOE
HFrEF (LVEF ≤40%)	I	A



HF type	COR	LOE
HFrEF (LVEF ≤40%)	1	A
HFmrEF (LVEF 41-49%)	2a	B-R
HFpEF (LVEF ≥50%)	2a	B-R



GDMT use, including SGLT2 inhibitors, is suboptimal³

^a2021 ESC HF guidelines recommend dapagliflozin or empagliflozin in patients with HFrEF to reduce the risk of hHF and death. These guidelines were released before full results of SGLT2 inhibitor trials in patients with HFmrEF or HFpEF, with or without T2D, were available.^{1,4-6}

1. McDonagh TA et al. *Eur Heart J*. 2021;42(36):3599-3726; 2. Heidenreich PA et al. *J Am Coll Cardiol*. 2022;79(17):e263-e421; 3. Ghazi L et al. *J Am Coll Cardiol*. 2022;79(22):2203-2213; 4. Anker SD et al. *N Engl J Med*. 2021;385:1451-1461; 5. Nassif ME et al. *Nat Med*. 2021;27:1954-1960; 6. Solomon SD et al. Online ahead of print. *N Engl J Med*. 2022.

Guida pratica ANMCO all'impiego degli inibitori del cotrasportatore sodio-glucosio di tipo 2 nei pazienti con scompenso cardiaco

Stefania Angela Di Fusco¹, Antonella Spinelli¹, Stefano Aquilani¹, Michele Massimo Gulizia²,
Domenico Gabrielli^{3,4}, Fabrizio Oliva⁵, Furio Colivicchi¹

Tabella 3. Considerazioni pratiche per l'impiego degli inibitori del cotrasportatore sodio-glucosio di tipo 2 nei pazienti con scompenso cardiaco e frazione di eiezione ridotta.

In chi e quando?	Indicazioni	Pazienti con HFrEF indipendentemente dalla presenza di DM2
	Controindicazioni	Gravidanza o allattamento eGFR <20 o 25 ml/min/1.73 m ² per empagliflozin e dapagliflozin rispettivamente <u>Ipoovolemia o PAS <95 mmHg</u> DM1 per mancanza di dati su efficacia e sicurezza Storia di chetoacidosi
Quale dosaggio?	Dapagliflozin Empagliflozin	Dose iniziale/di mantenimento 10 mg/die Dose iniziale/di mantenimento 10 mg/die
Come usarli?	Definire la funzione renale all'inizio della terapia e monitorarla regolarmente Monitorare la glicemia (soprattutto nei pazienti diabetici) Identificare eventuali fattori di rischio per chetoacidosi ed eliminarli <u>Monitorare regolarmente il bilancio di liquidi, particolarmente se il paziente assume diuretici, se è anziano o fragile</u>	
Effetti collaterali	Glicosuria: predisposizione ad infezioni fungine genito-urinarie Ipoglicemia: usare con cautela in associazione a insulina, sulfoniluree e altri insulino-secretagoghi <u>Ipotensione: valutare lo stato di idratazione e ridurre o sospendere eventuale terapia diuretica in atto</u> Chetoacidosi: da sospettare in caso di nausea, vomito, anoressia, dolore addominale, sete eccessiva, difficoltà a respirare, confusione, insolita fatica Fascite necrotizzante del perineo o gangrena di Fournier	

DM1, diabete mellito di tipo 1; DM2, diabete mellito di tipo 2; eGFR, filtrato glomerulare stimato; HFrEF, scompenso cardiaco con frazione di eiezione ridotta; PAS, pressione arteriosa sistolica.

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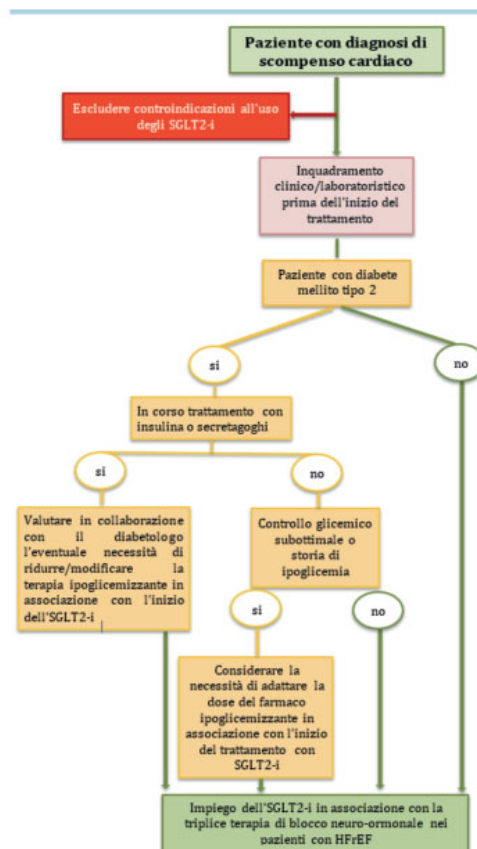
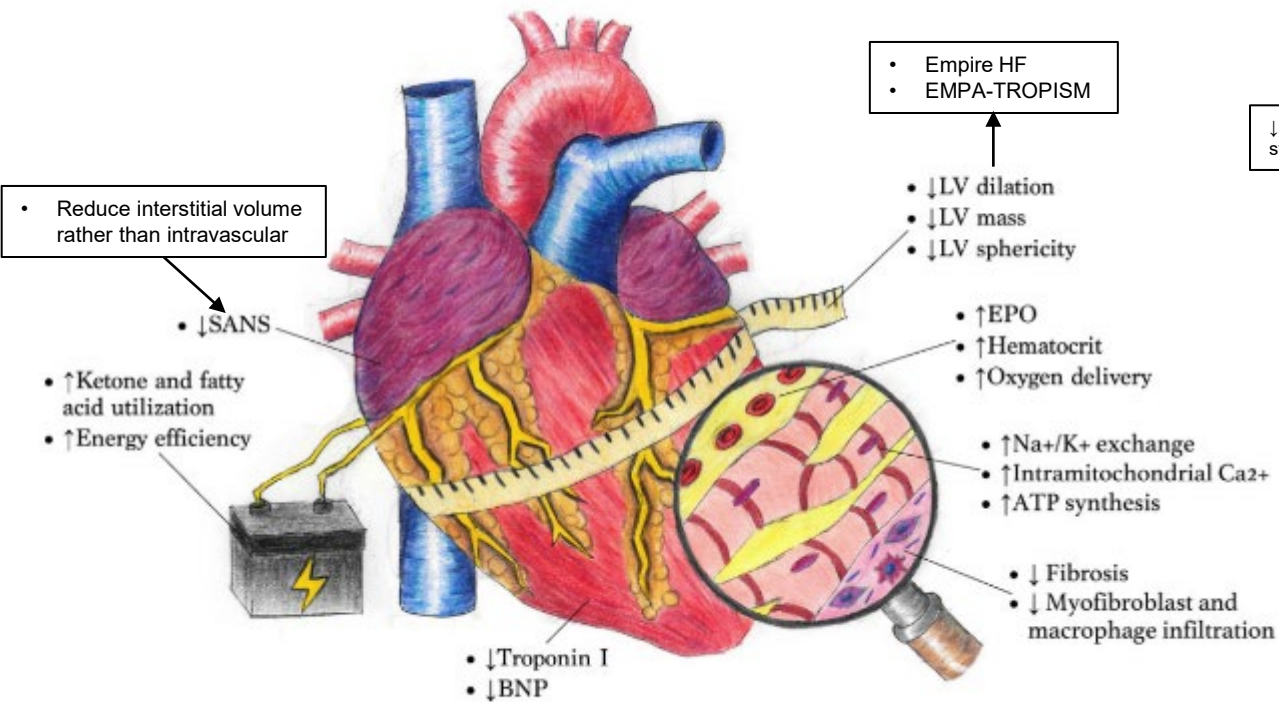


Figura 2. Algoritmo per l'impiego degli inibitori del cotrasportatore sodio-glucosio di tipo 2 (SGLT2-i) nei pazienti con scompenso cardiaco.
HFrEF, scompenso cardiaco con frazione di eiezione ridotta (<40%).
Modificata da Di Fusco et al.²²

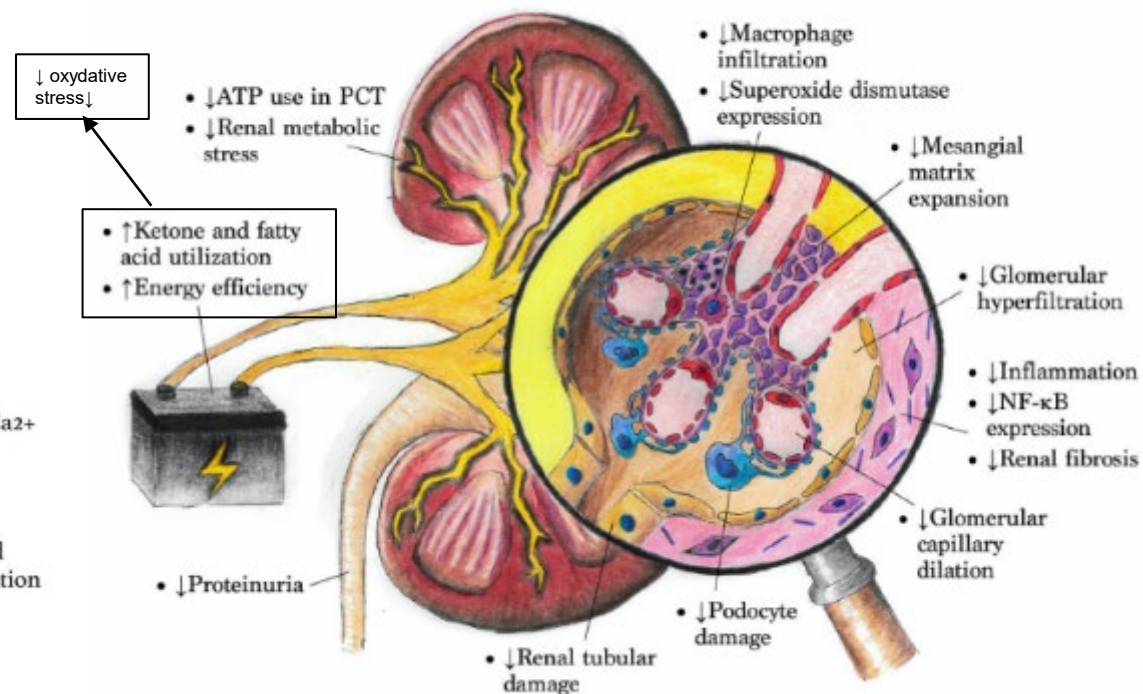
Cardio-Renal Mechanisms of benefit of SGLT2 inhibitors

Cardiac Mechanisms of Benefit of SGLT2 Inhibitors



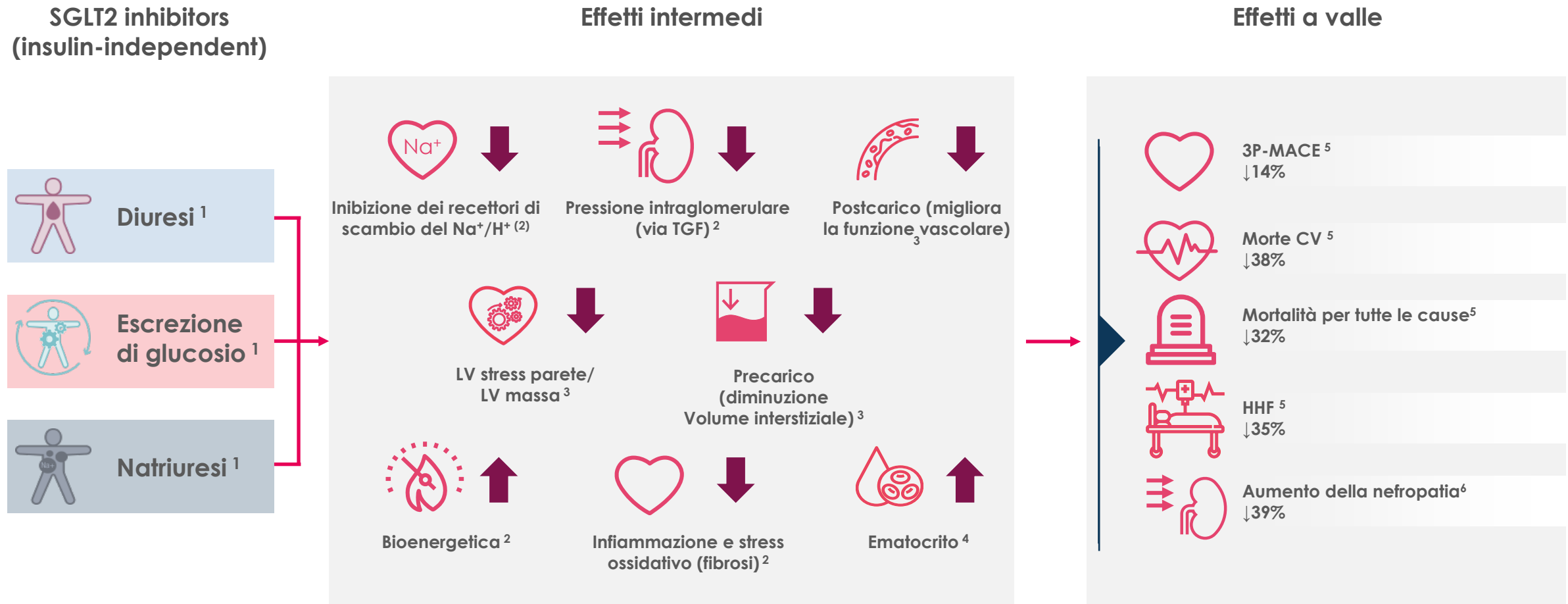
EPO= Erythropoietin, LV= Left ventricular, SANS= Sympathetic autonomic nervous system

Renal Mechanisms of Benefit of SGLT2 Inhibitors



ATP= Adenosine triphosphate, NF-κB = Nuclear factor κB, PCT= Proximal convoluted tubule

Gli effetti degli inibitori SGLT2 sul sistema cardio-renale-metabolici possono essere mediati da molteplici meccanismi



SGLT2: sodium-glucose cotransporter 2; LV: left ventricular; HHF: hospitalisation for heart failure; TGF: tubuloglomerular feedback

1. Giugliano et al. Cardiovasc Diabetol (2021) 20:17; 2. Barutta et al., Diabetes Metab Res Rev. 2019;e3171; 3. Margonato D et al., Heart Failure Reviews (2021) 26:337–

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5. Zinman B et al. N Engl J Med 2015;373:2117; 6. Wanner C et al. N Engl J Med 2016;375:323



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Braunwald's Corner

SGLT2 inhibitors: the statins of the 21st century

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A relatively small number of drugs have been responsible for major advances in medical practice. The discovery, development, and elucidation of the mechanisms of action of aspirin, penicillin, and statins are remarkable success stories, each with some surprises and each crowned by a Nobel Prize. The sodium glucose co-transporter inhibitors have been proven effective in the treatment of type 2 diabetes mellitus, various forms of heart failure, and kidney failure and represent the, or one of the major pharmacological advances in cardiovascular medicine in the 21st century.

Grazie

