

CONGRESSO REGIONALE
CONGIUNTO **SID-AMD**
PIEMONTE | VALLE D'AOSTA 2023



SINFONIA 2.0 PER IL DIABETE: *prove d'orchestra*

Scompenso cardiaco acuto: uso precoce degli SGLT2-i ?

Simone Frea

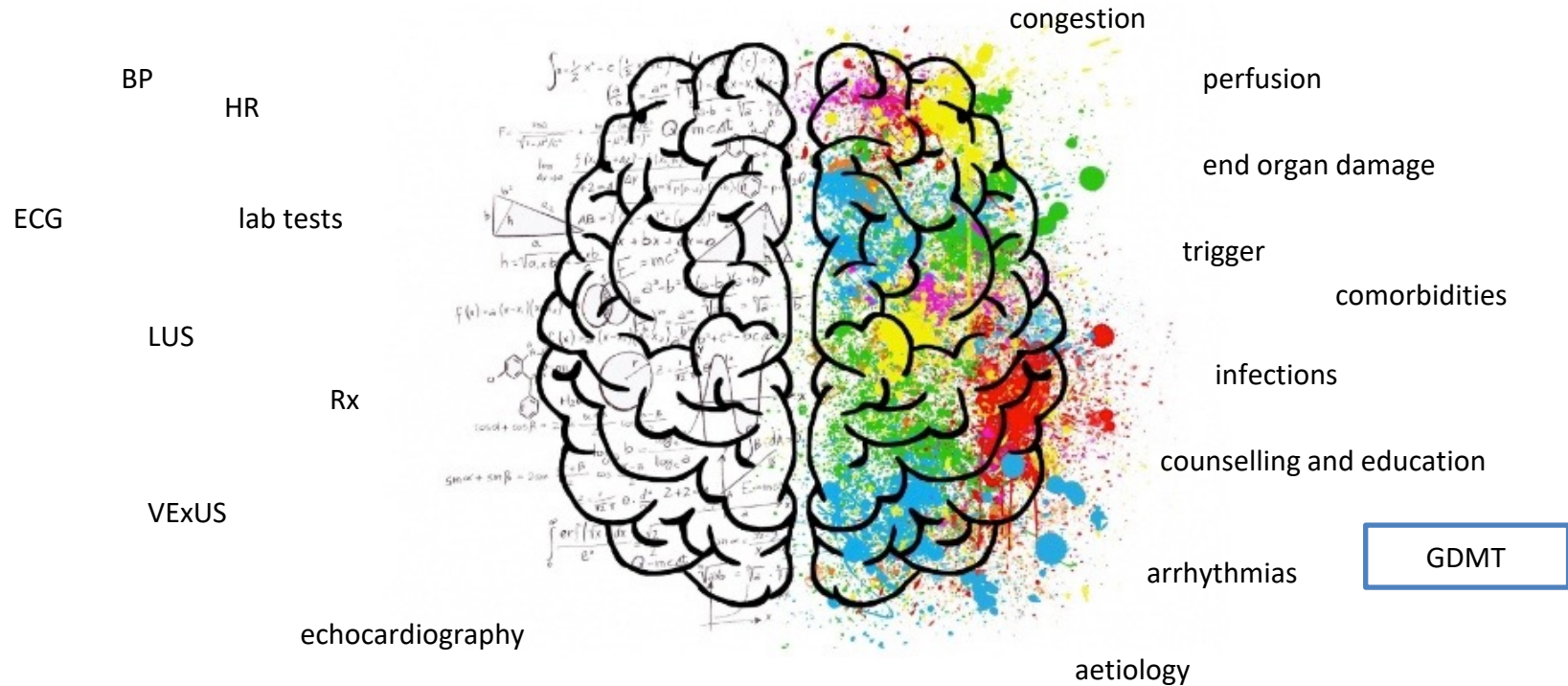
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Città della Salute e della Scienza Hospital



disclosure

none

GDMT in acute heart failure setting ?



Main concerns and issues about GDMT in acute HF

low blood pressure

worsening heart failure

worsening renal function

echocardiographic “dependency”

infections

critical illness and withdrawal

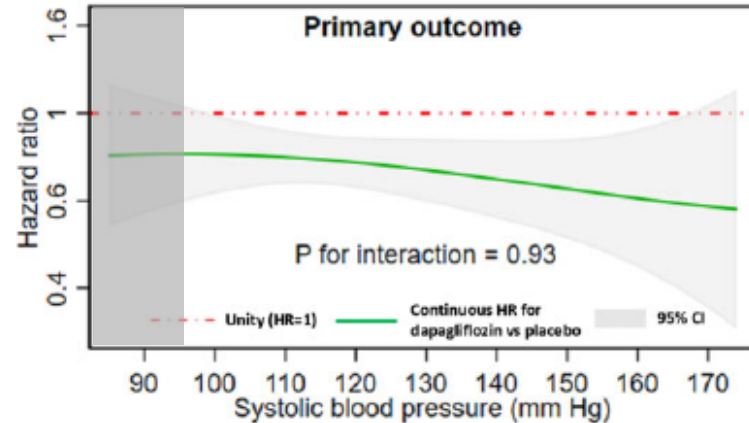
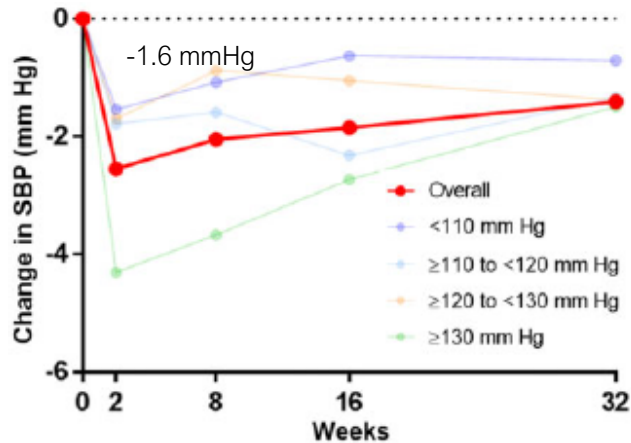
SGLT2-i in acute HF?

low blood pressure

SGLT2I and low blood pressure

4474 outpatients HFrEF

placebo-corrected change in SBP by baseline SBP category



Effect of dapagliflozin according to baseline systolic blood pressure in the Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure trial (DAPA-HF)

European Heart Journal (2020) 41, 3402–3418

SGLT2-i in acute HF?

low blood pressure

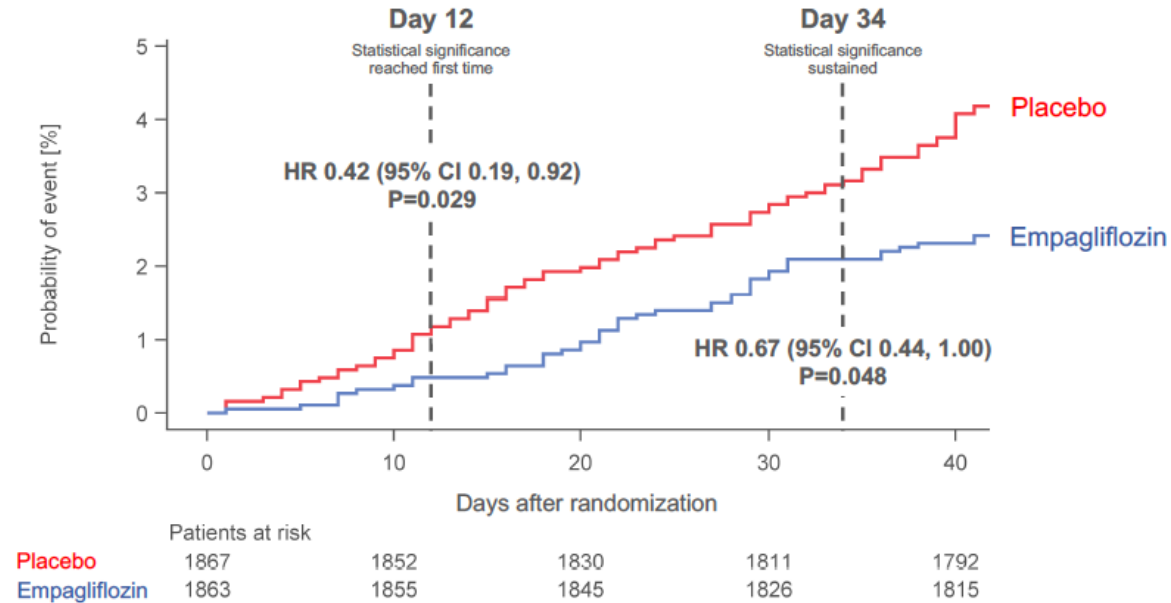
worsening heart failure

SGLT2i and Worsening heart failure

Effect of Empagliflozin on the Clinical Stability of Patients With Heart Failure and a Reduced Ejection Fraction

The EMPEROR-Reduced Trial

3730 outpatients HFrEF

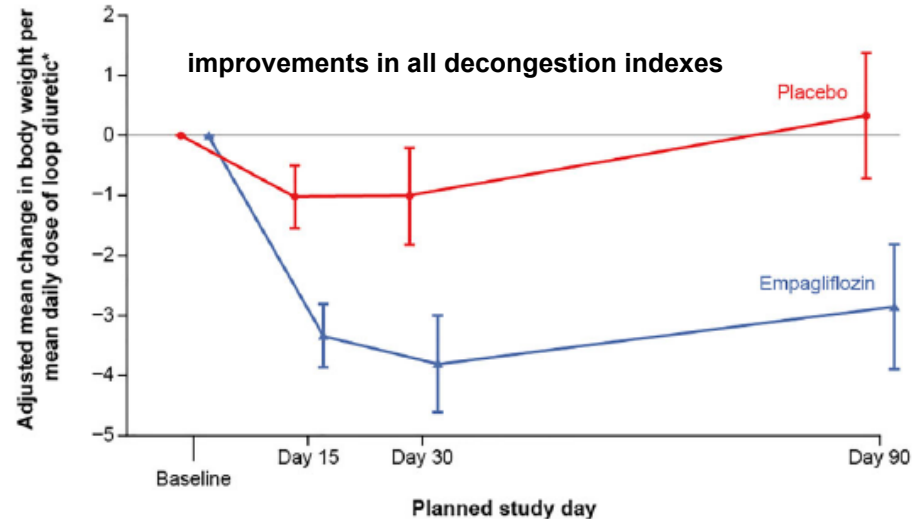


empagliflozin and worsening heart failure

Impact of empagliflozin on decongestion in acute heart failure: the EMPULSE trial

530 inpatients (ADHF, eGFR > 20 ml/min/1.73 m²)

empagliflozin 10 mg 1-5 days from hospitalization



Patients at risk

Placebo	200	194	180	165
Empagliflozin	195	181	183	171

Initiation of empagliflozin in AHF patients after initial in-hospital stabilization resulted in an early, effective and sustained improvements in all decongestion indexes, which was associated with clinical benefit at Day 90.

dapagliflozin and worsening heart failure

Safety and Efficacy of Adding Dapagliflozin to Furosemide in Type 2 Diabetic Patients With Decompensated Heart Failure and Reduced Ejection Fraction

Ayman Ibrahim¹, Ramadan Ghaleb¹, Hossam Mansour¹, Amr Hanafy¹, Naggeh M. Mahmoud¹, Mohamed Abdelfatah Elsharef¹, Mohamed Kamal Salama¹, Saud M. Elsaughier¹, Lobna Abdel-Wahid², Mona Embarek Mohamed³, Ahmed K. Ibrahim⁴ and Ahmed Abdel-Galeel^{5*}

100 inpatients (ADHF, EF < 40%)

improvements in diuretic response

TABLE 2 | Change associated with diuresis in the studied population.

Parameter	Control Group (n = 50)	Study Group (n = 50)	P-value*
Urine output in liters (mean ± SD)	14.43 ± 0.7	18.46 ± 0.5	< 0.001*
Fluid intake in liters (mean ± SD)	7.01 ± 0.3	7.52 ± 0.2	0.139*
Total fluid balance in liters (mean ± SD)	-7.42 ± 0.7	-10.94 ± 0.4	< 0.001*
Fluid loss/diuretics in ml/mg (mean ± SD)	19.49 ± 1.2	34.75 ± 2.2	< 0.001*
Fluid balance/diuretics ml/mg (mean ± SD)	-9.87 ± 0.6	-20.86 ± 1.0	< 0.001*
Furosemide use			
Total dose in mg (mean ± SD)	855.00 ± 74.8	597.60 ± 34.4	0.002*
Dose/day (mean ± SD)	170.78 ± 9.7	126.07 ± 4.3	< 0.001*
Diuretic response in Kg/40mg furosemide (mean ± SD)	-0.042 ± 0.03	-0.089 ± 0.04	< 0.001*

*Independent t-test test was used to compare the mean difference between groups.

SGLT2i and Worsening heart failure and diuretic response

Lack of durable natriuresis and objective
decongestion following SGLT2 inhibition
in randomized controlled trials of patients
with heart failure

Milton Packer^{1*}

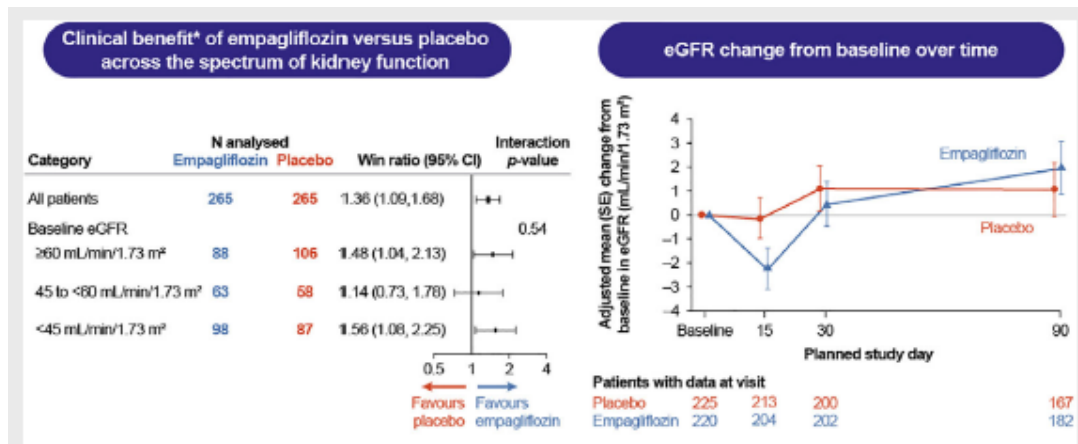
SGLT2-i in acute HF?

low blood pressure

worsening heart failure

worsening renal function

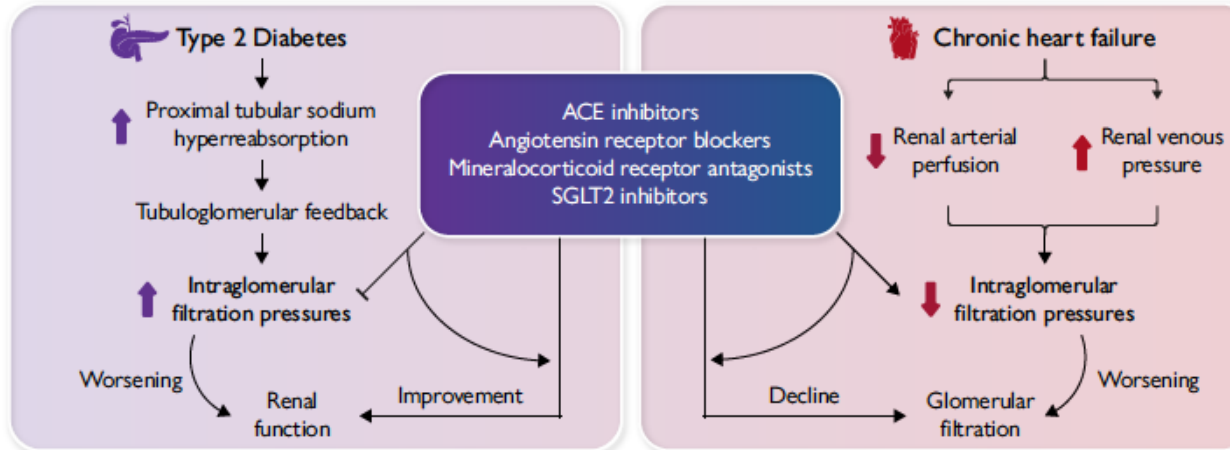
SGLT2-i and Worsening renal function



Renal effects of empagliflozin in patients hospitalized for acute heart failure: from the EMPULSE trial

SGLT2-i and Worsening renal function

End-stage kidney disease					
	Placebo		SGLT2 inhibitor		Hazard Ratio (95% CI)
	Events	Total	Events	Total	
DAPA-HF	16	2,372	16	2,370	1.00 (0.50–1.99)
EMPEROR-Reduced	12	1,867	6	1,863	0.50 (0.19–1.33)
EMPEROR-Preserved	16	2,991	20	2,997	1.25 (0.65–2.42)
DELIVER	20	3,131	14	3,131	0.70 (0.35–1.39)
Total	64	10,361	56	10,361	0.88 (0.61–1.26)



SGLT2-i in acute HF

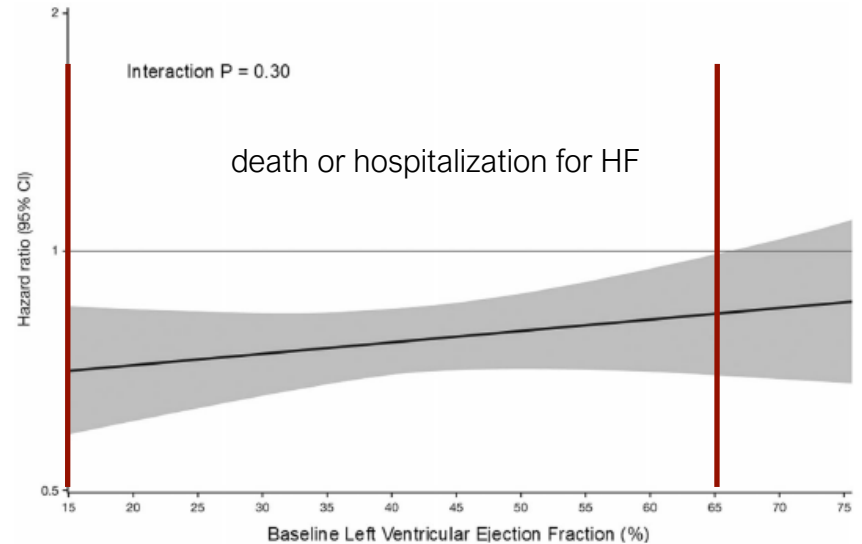
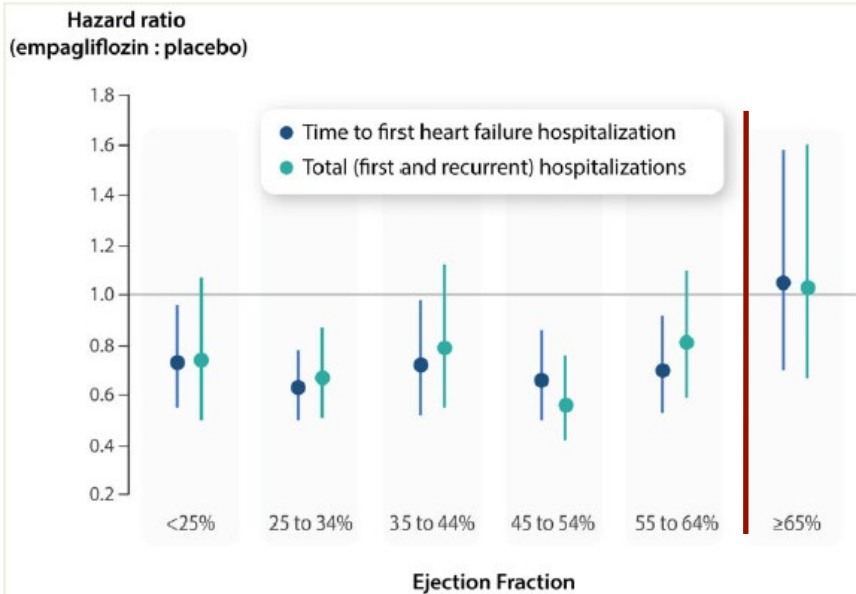
low blood pressure

worsening heart failure

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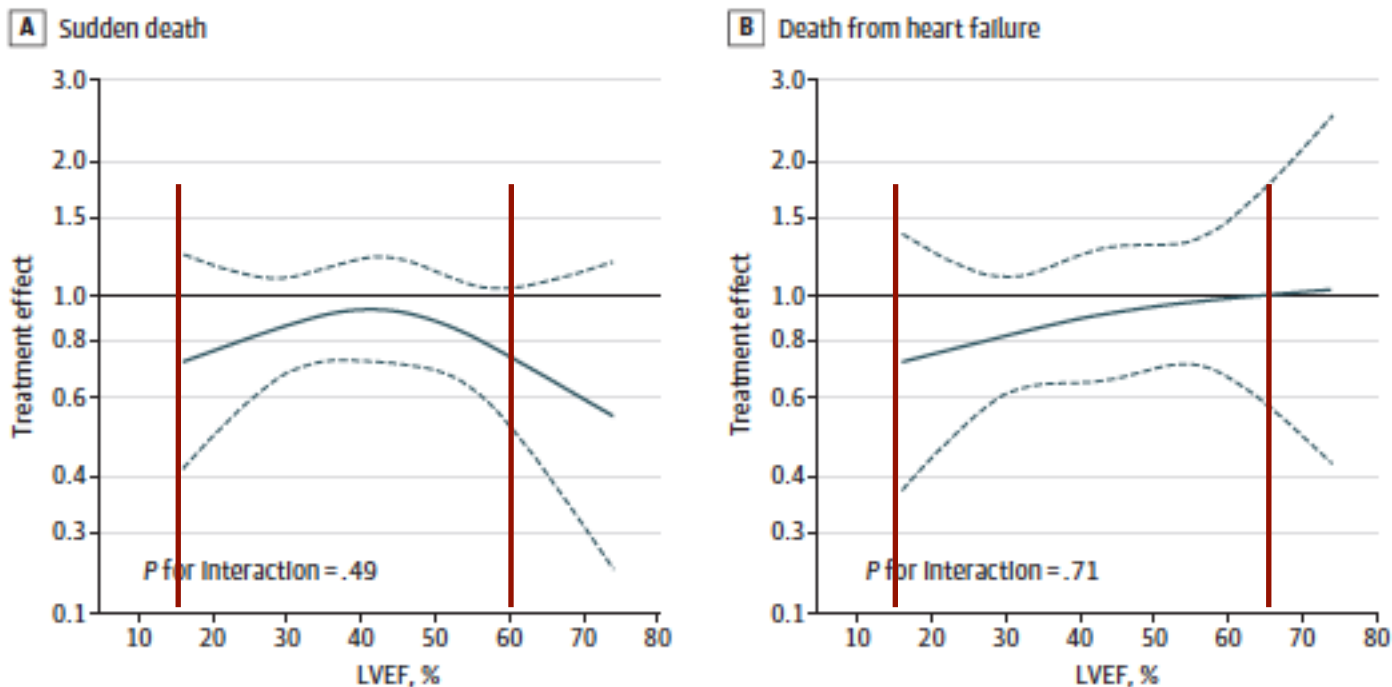
echocardiographic “dependency”

“echocardiographic independency” of empagliflozin



Effect of empagliflozin in patients with heart failure across the spectrum of left ventricular ejection fraction

“echocardiographic independency” of dapagliflozin



JAMA Cardiology | Original Investigation

Effect of Dapagliflozin on Cause-Specific Mortality in Patients With Heart Failure Across the Spectrum of Ejection Fraction
A Participant-Level Pooled Analysis of DAPA-HF and DELIVER

SGLT2-i in acute HF

low blood pressure

worsening heart failure

worsening renal function

echocardiographic “dependency”

infections

SGLT2i and infections

The SGLT2 inhibitor empagliflozin in patients hospitalized for acute heart failure: a multinational randomized trial

EMPULSE trial: 524 ADHF inpatients

SUPPLEMENTARY TABLE 3. DETAILS ON RENAL AND URINARY ADVERSE EVENTS

MedDRA PT	Empagliflozin 10 mg		Placebo	
	N (%)	Rate/100 pt-yrs	N (%)	Rate/100 pt-yrs
Number of patients	260 (100.0)		264 (100.0)	
Acute renal failure (narrow SMQ) ¹	20 (7.7)	34.69	32 (12.1)	55.69
Acute kidney injury	10 (3.8)	16.90	19 (7.2)	32.28
Renal impairment	9 (3.5)	15.38	11 (4.2)	18.58
Renal failure	2 (0.8)	3.34	2 (0.8)	3.33
Serious	12 (4.6)	20.37	23 (8.7)	39.35
Leading to discontinuation of study medication	6 (2.3)	10.02	4 (1.5)	6.64
Urinary tract infection	11 (4.2)	18.80	17 (6.4)	29.23
Cystitis	8 (3.1)	13.62	5 (1.9)	8.36
Urinary tract infection	3 (1.2)	5.01	6 (2.3)	10.10
Urinary tract infection bacterial	1 (0.4)	1.67	6 (2.3)	10.07
Escherichia urinary tract infection	1 (0.4)	1.67	0	-
Bacteriuria	0	-	1 (0.4)	1.66
Complicated ²	1 (0.4)	1.67	2 (0.8)	3.33

¹ Using standard MedDRA query v24.0 definition for Acute renal Failure consist of 19 preferred terms including acute kidney injury, subacute kidney injury, anuria, oliguria, azotemia, renal failure, renal impairment, haemodialysis, haemofiltration, peritoneal dialysis

² Complicated UTI: Renal infections or Urosepsis or serious urinary tract infections.

SGLT2-i in acute HF

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critical illness and withdraw

SGLT2-i in critical illness

It should be considered to interrupt SGLT-2 inhibitor therapy for at least 3 days before intermediate- and high-risk NCS.

Ila

C

bivACM, no DM -> denervazione toracoscopia -> acidosi + PAS 60 mmHg “calda” non responsiva a dobutamina

Misurati (37.0C)

pH	7.21	
pCO ₂	38	mmHg
pO ₂	86	mmHg
Na ⁺	130	mmol/L
K ⁺	5.1	mmol/L
Ca ⁺⁺	1.14	mmol/L
Glu	66	mg/dL
Lat	0.9	mmol/L
Hct	44	%

Parametri derivati

Ca ⁺⁺ (7.4)	1.05	mmol/L
HC03 ⁻	15.2	mmol/L
HC03std	15.6	mmol/L
TC02	16.4	mmol/L
BEecf	-12.7	mmol/L
BE(B)	-11.9	mmol/L
S02c	94	%
THbc	13.6	g/dL

pH	7.28	
pCO ₂	39	mmHg
pO ₂	111	mmHg
Na ⁺	130	mmol/L
K ⁺	4.6	mmol/L
Cl ⁻	97	mmol/L
Ca ⁺⁺	1.16	mmol/L
Hct	37	%
Glu	103	mg/dL
Lac	0.8	mmol/L
BEecf	-8.4	mmol/L
tHb(c)	12.6	g/dL

Urine

Urine - Esame Chimico/Fisico

Aspetto	limpido	
Colore	giallo paglierino	
pH	5.5	5.5 - 6.5
Glucosio	> 1000	mg/dL < 10
Albumina	0	mg/dL < 10
HB-perossidasi	0.00	mg/dL 0.00
Corpi chetonici	80	mg/dL 0
Bilirubina	0.0	mg/dL 0.0
Urobilinogeno	0.2	mg/dL 0.2 - 1.0
Esterasi leucocitaria	0	num/gL < 25
Nitriti	Assenti	
Peso specifico	1.015	1.005 - 1.028

Urine - Esame Microscopico (c.m. 400 x)

nessuna di patologia da segnalare

- SGLT2-i

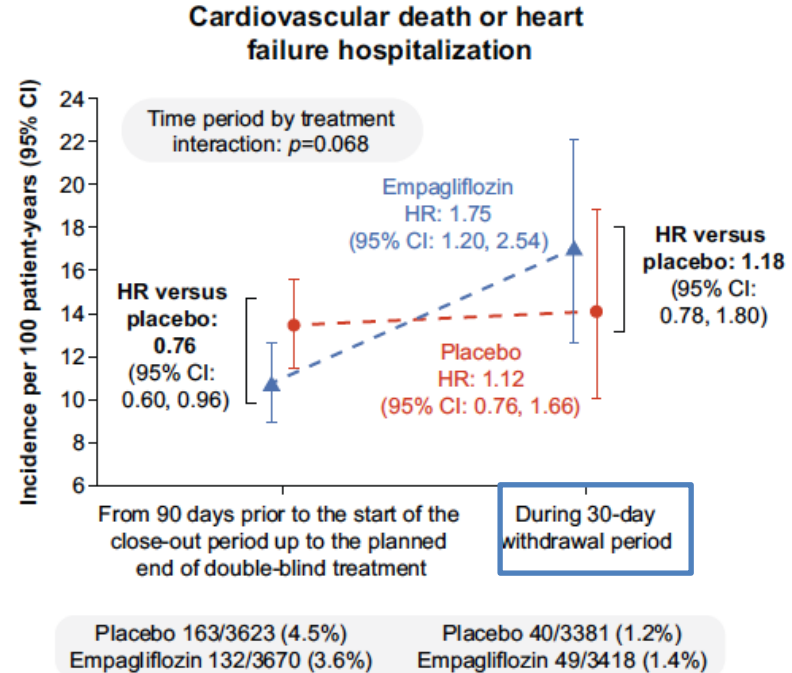
idrocortisone (etomidate)

SGLT2-i withdrawal

Blinded Withdrawal of Long-Term Randomized Treatment With Empagliflozin or Placebo in Patients With Heart Failure

Milton Packer¹, MD; Javed Butler², MD, MPH, MBA; Cordula Zeller³, Dipl. Math.; Stuart J. Pocock⁴, PhD; Martina Brueckmann⁵, MD; João Pedro Ferreira⁶, MD; Gerasimos Filippatos⁷, MD; Muhammad Shariq Usman, MD; Faiez Zannad⁸, MD, PhD; Stefan D. Anker⁹, MD, PhD

3981 patients from EMPEROR-Reduced and Preserved



SGLT2-i in acute HF

low blood pressure	SBP > 95 mmHg		
worsening HF	improve decongestion (de novo)		
worsening renal function		mild, transient, less than ARNI/ACE	
EF independency	15-65%		
urinary infections			
critical illness			euDKA (at home?)

grazie

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