

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

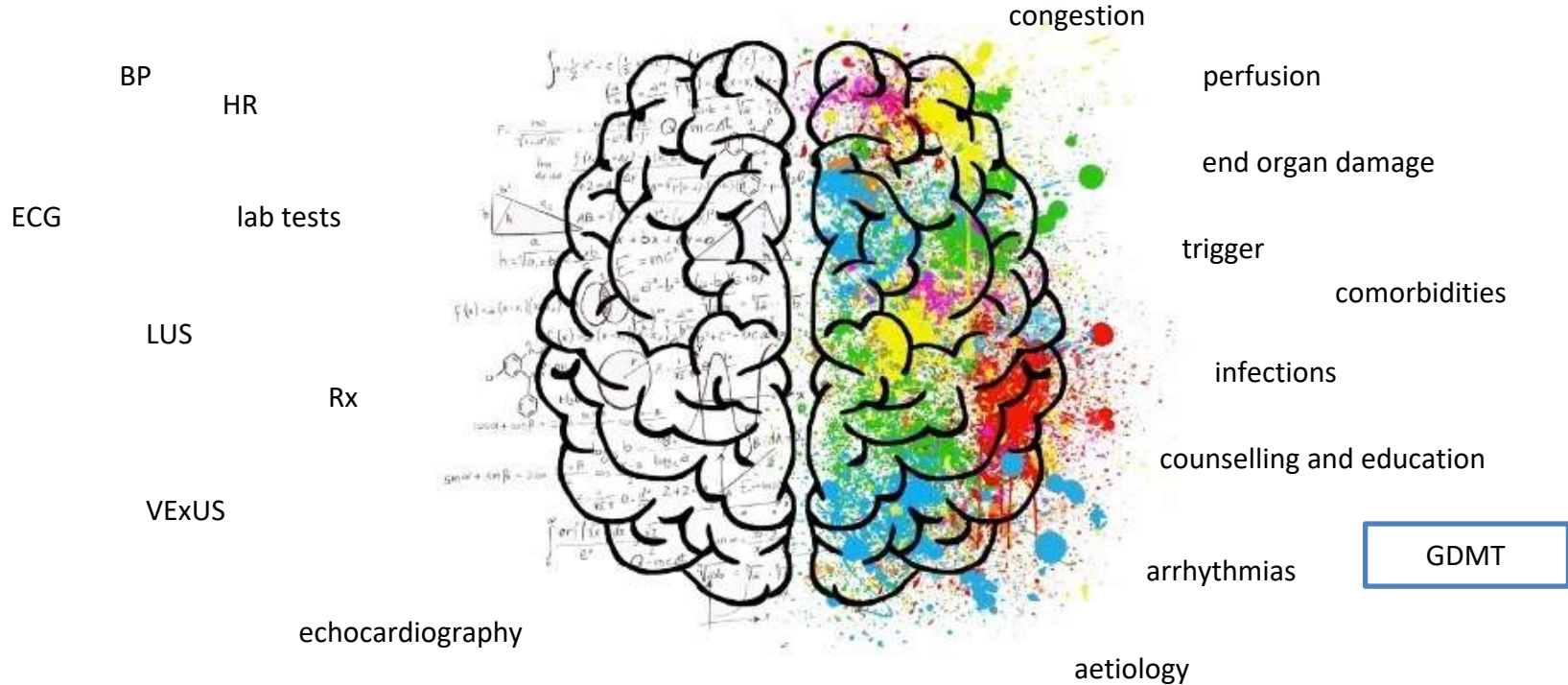
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**disclosure**

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

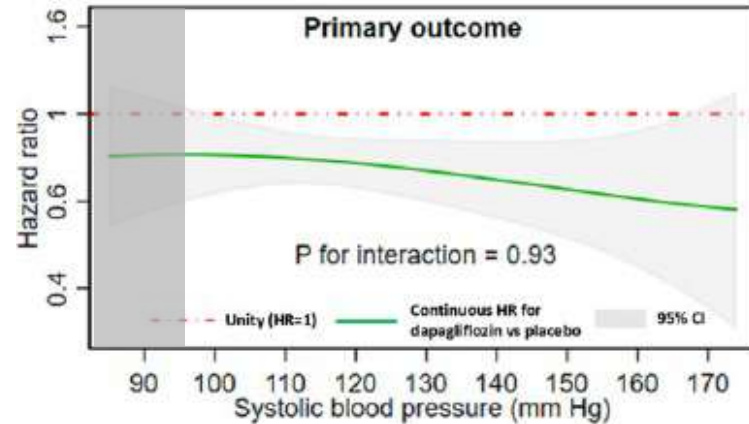
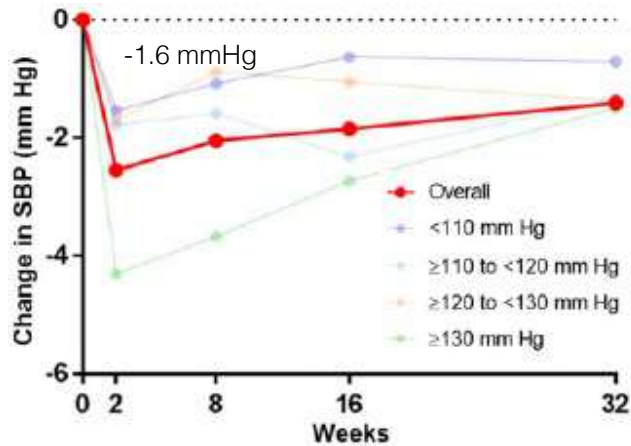
# SGLT2-i in acute HF?

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

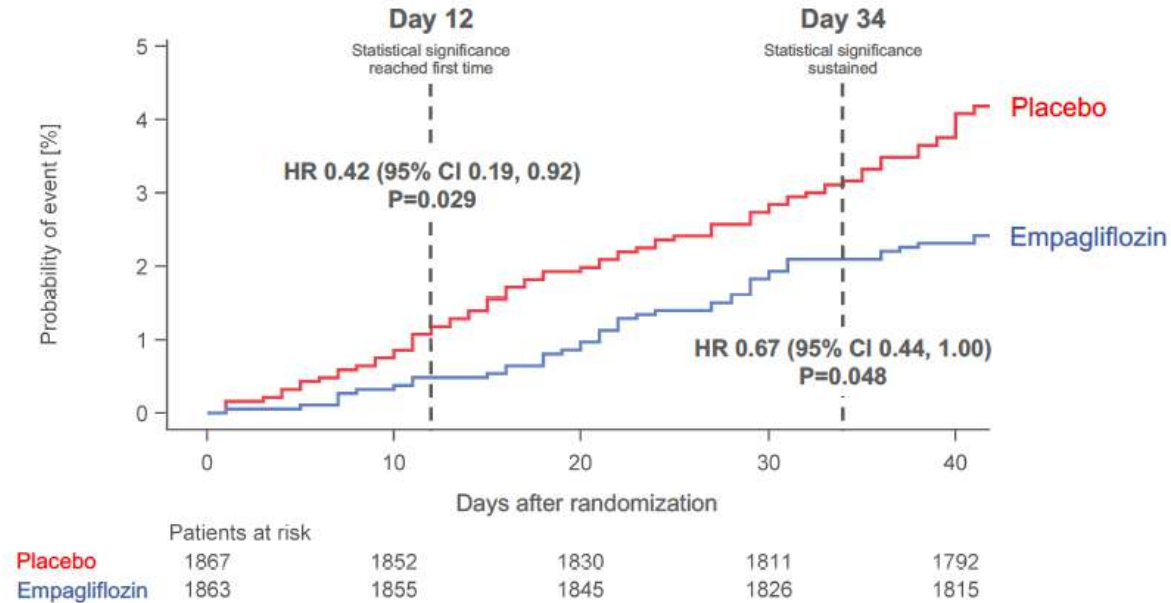
worsening heart failure

# 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



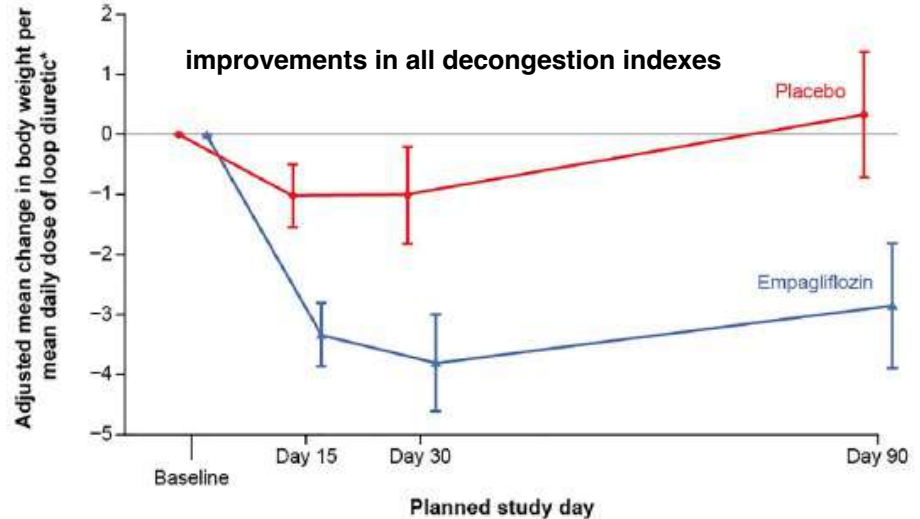


# empagliflozin and worsening heart failure

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

530 inpatients (ADHF, eGFR > 20 ml/min/1.73 m<sup>2</sup>)

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 Ibrahim<sup>1</sup>, Ramadan Ghalob<sup>1</sup>, Hossam Mansour<sup>1</sup>, Amr Hanafy<sup>1</sup>, Naggeh M. Mahmoud<sup>1</sup>, Mohamed Abdelfatah Elsharef<sup>1</sup>, Mohamed Kamal Salama<sup>1</sup>, Saud M. Elsaugnier<sup>1</sup>, Lobna Abdel-Wahid<sup>2</sup>, Mona Embarek Mohamed<sup>3</sup>, Ahmed K. Ibrahim<sup>4</sup> and Ahmed Abdel-Galeel<sup>5\*</sup>

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*
<b>Furosemide use</b>			
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<sup>1\*</sup>

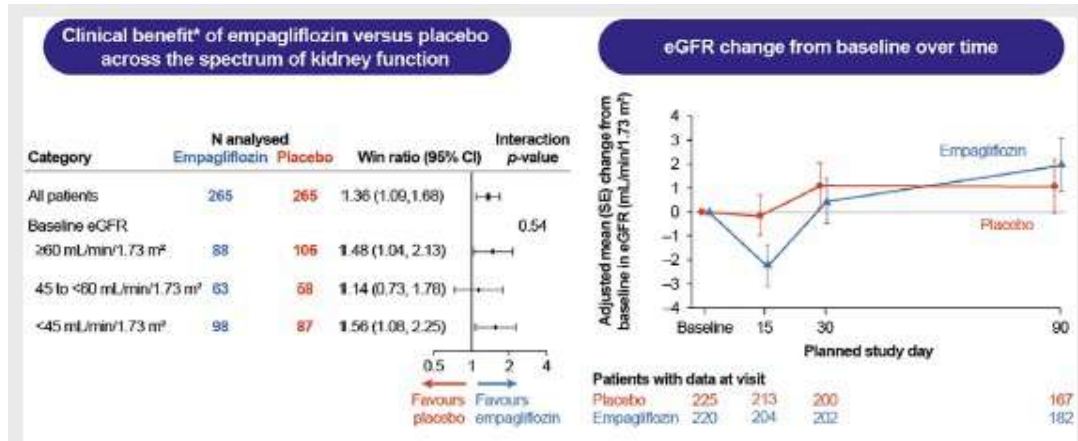
## SGLT2-i in acute HF?

low blood pressure

worsening heart failure

worsening renal function

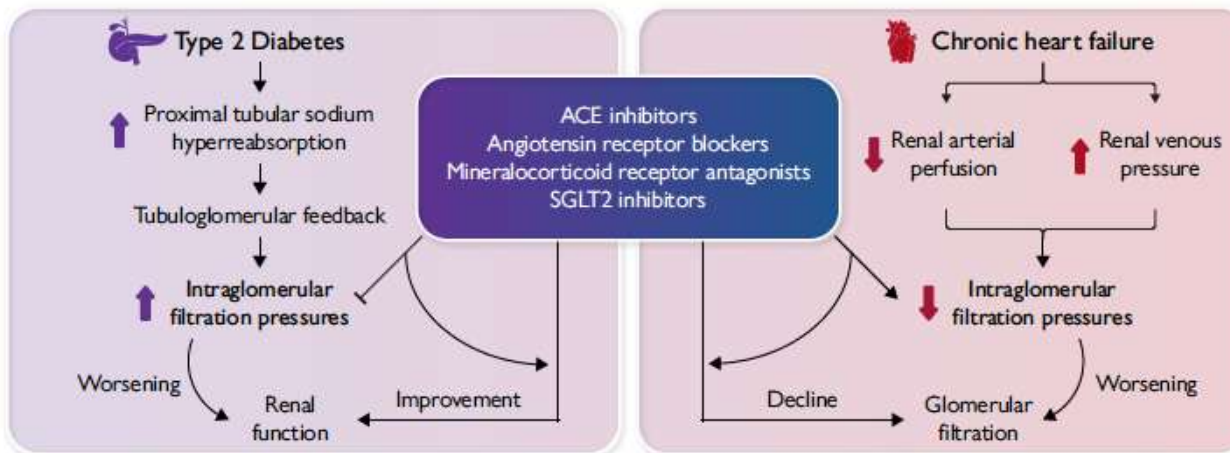
# SGLT2-i and Worsening renal function



**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)
<b>Total</b>	<b>64</b>	<b>10,361</b>	<b>56</b>	<b>10,361</b>	<b>0.88 (0.61–1.26)</b>



# SGLT2-i in acute HF

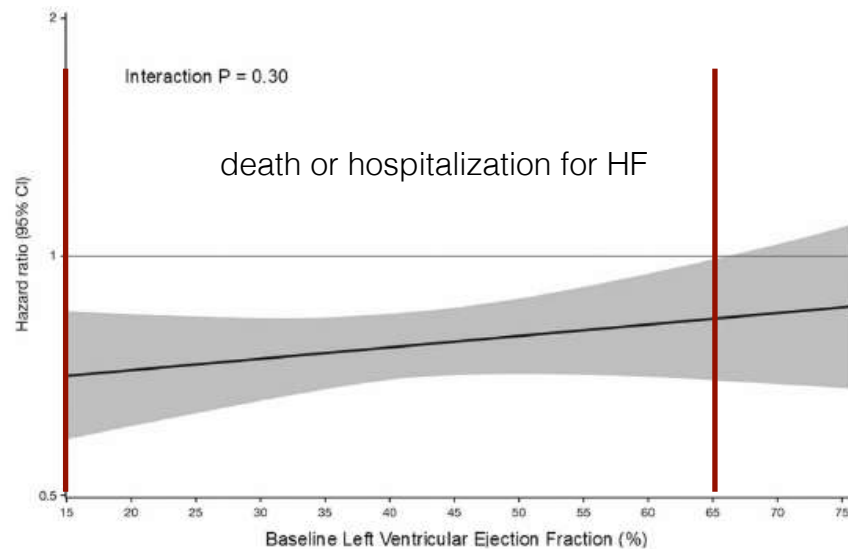
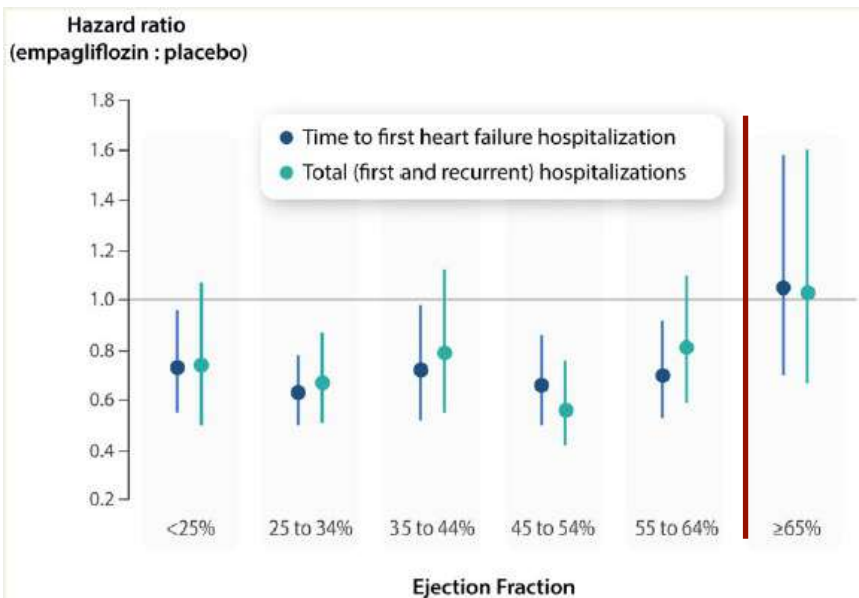
low blood pressure

worsening heart failure

worsening renal function

echocardiographic “dependency”

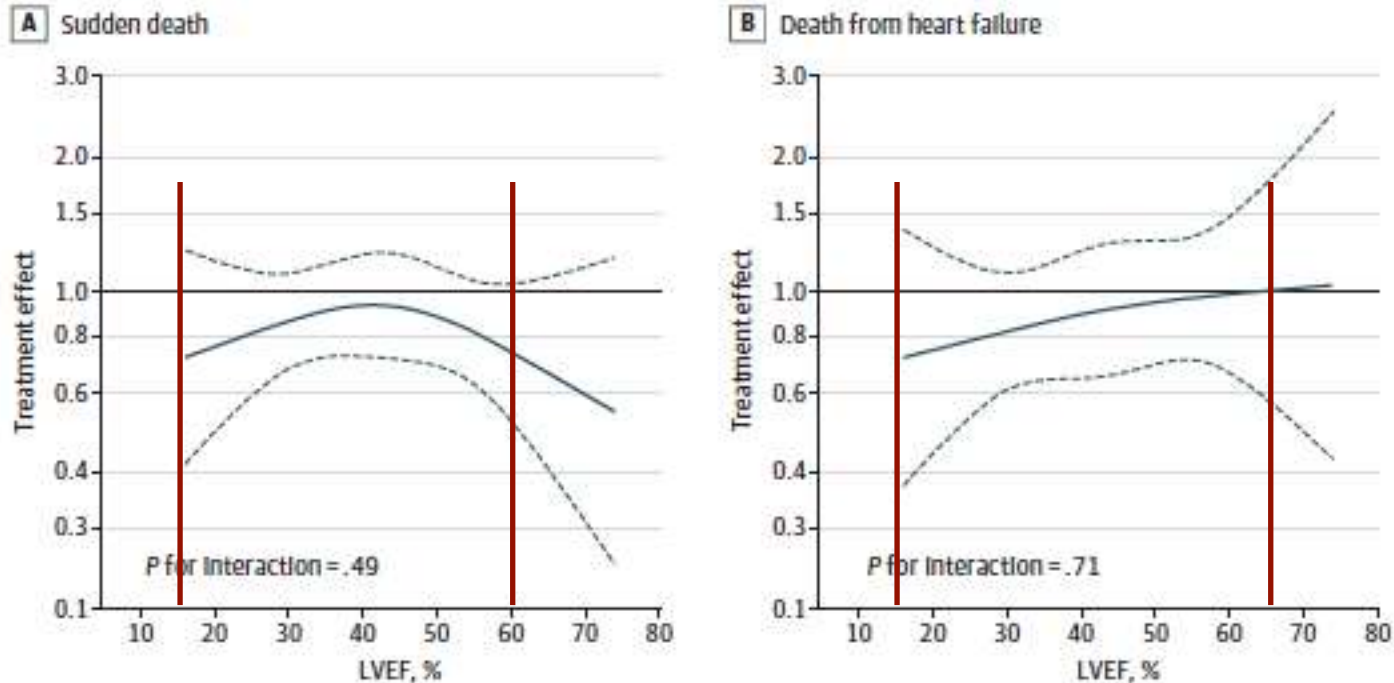
# “echocardiographic independency” of empagliflozin



**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

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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) <sup>1</sup>	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 <sup>2</sup>	1 (0.4)	1.67	2 (0.8)	3.33

<sup>1</sup> 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

<sup>2</sup> Complicated UTI: Renal infections or Urosepsis or serious urinary tract infections.

# SGLT2-i in acute HF

low blood pressure

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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 <sub>2</sub>	38	mmHg
pO <sub>2</sub>	86	mmHg
Na+	130	mmol/L
K+	5.1	mmol/L
Ca <sup>++</sup>	1.14	mmol/L
Glu	66	mg/dL
Lat	0.9	mmol/L
Hct	44	%

Parametri derivati

Ca <sup>++</sup> (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 <sub>2</sub>	39	mmHg
pO <sub>2</sub>	111	mmHg
Na <sup>+</sup>	130	mmol/L
K <sup>+</sup>	4.6	mmol/L
Cl <sup>-</sup>	97	mmol/L
Ca <sup>++</sup>	1.16	mmol/L
Hct	37	%
Glu	103	mg/dL
Lac	0.8	mmol/L
BEecf	-8.4	mmol/L
THbc	12.6	g/dL

Urine

Urine - Esame Chimico/Fisico

Aspetto	
Colore	
pH	
Glucosio	
Albumina	
HB-perossidasi	
Corpi chetonici	
Bilirubina	
Urobilinogeno	
Esterasi leucocitaria	
Nitriti	
Peso specifico	
Urine - Esame Microscopico (c.m. 400 x)	

limpido	
giallo paglierino	
5.5	
> 1000	
0	
0.00	
0.00	
0.0	
0.0	
0.2	
0	
Assenti	
1.015	

mg/dL	5.5 - 6.5
mg/dL	< 10
mg/dL	< 10
mg/dL	0.00
mg/dL	0
mg/dL	0.0
mg/dL	0.2 - 1.0
num/L	< 25
	1.005 - 1.028

nulla di patologico da segnalare

**- SGLT2-i**

**idrocortisone (etomidate)**

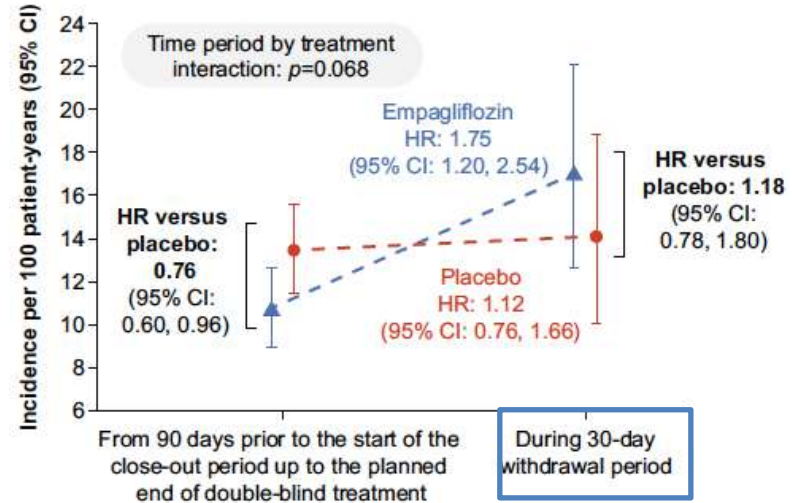
# SGLT2-i withdrawal

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

Milton Packer MD; Javed Butler MD, MPH, MBA; Cordula Zeller Dipl. Math.; Stuart J. Pocock PhD; Martina Brueckmann MD; João Pedro Ferreira MD; Gerasimos Filippatos MD; Muhammad Shariq Usman, MD; Faleh Zannad MD, PhD; Stefan D. Anker MD, PhD

**3981 patients** from EMPEROR-Reduced and Preserved

### Cardiovascular death or heart failure hospitalization



Placebo 163/3623 (4.5%)	Placebo 40/3381 (1.2%)
Empagliflozin 132/3670 (3.6%)	Empagliflozin 49/3418 (1.4%)

# 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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