

SGLT2is: Are they a Miracle For Cancer- Associated Nephrotoxicity Too?

Onconeurology Symposium

Continuing Education

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Disclosure of Interest

- **Contracted consulting fees and travel support for contracted activities:** from AstraZeneca, IOTsuka, Novo Nordisk, GSK, Sanofi, Boehringer, Vifor CSL, Otsuka, ICU Medical, Bayer.
- **Grants:** from Boehringer Ingelheim, Instituto de Salud Carlos III, Fundación Senefro and Ministerio de Ciencia e Innovación, Marató TV3, ERA PerMed2022.
- **Received fees for consultation:** from AstraZeneca, Novo Nordisk, Boehringer, CSL Vifor, Otsuka, GBayer.

Learning Objectives

- To understand the potential cardio-renal protective effects of SGLT2 inhibitors in patients with cancer.
- To review the role and expression of SGLT2 in cancer and its potential therapeutic implications.
- To explore the mechanisms underlying the potential anti-tumoral and nephroprotective effects of SGLT2 inhibitors.
- To discuss the emerging evidence on SGLT2 inhibitors for preventing cancer-associated nephrotoxicity.

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- **Conclusions**

Introduction

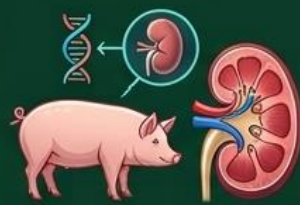
A DECADE OF REVOLUTIONARY ADVANCES IN RENAL HEALTH (2016-2026) TOP 10 DISCOVERIES IN NEPHROLOGY (LAST 10 YEARS)

1. SGLT2 INHIBITORS



- Protect the kidney and the heart.
- Slow the progression of chronic kidney disease (CKD).

2. XENOTRANSPLANTATION



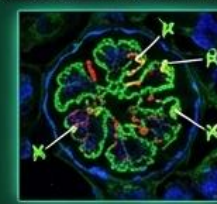
- Advances with genetically-edited porcine organs.
- Overcoming rejection to alleviate the organ shortage.

3. RENAL LIQUID BIOPSY



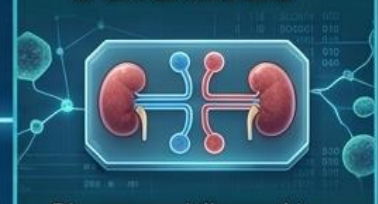
- DNA and RNA analysis in blood/urine.
- Non-invasive diagnosis and monitoring of renal diseases.

4. COMPLEMENT IN GLOMERULOPATHIES



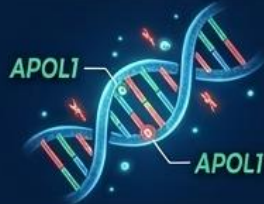
- Targeted therapies against the complement system.
- New treatments for C3G, aHUS, and IgA Nephropathy.

5. KIDNEY-ON-A-CHIP & ORGANIDS



- Disease modeling and in vitro drug testing.
- Replicating human renal physiology to reduce animal testing.

6. PRECISION GENETICS & APOL1



- Identification of specific risks based on ancestry.
- Targeted therapies against APOL1 risk variants.

7. 3D BIOPRINTING OF RENAL TISSUE



- Creation of functional renal structures.
- Steps toward the bioengineering of whole organs.

8. NEXT-GENERATION DIALYSIS



- More selective and biocompatible filtration membranes.
- Portable technologies and home dialysis.

9. ARTIFICIAL INTELLIGENCE IN NEPHROLOGY



- Early detection and prediction of CKD progression.
- Optimization of drug dosing and clinical alerts.

10. NEW BIOMARKERS OF ACUTE INJURY



- NGAL
- KIM-1, anti-PLA2R
- Ultra-early detection of acute renal failure.
- Improving results after surgery or trauma.

#Nephrology

#Nephrology #MedicalAdvances #LastDecade #RenalHealth

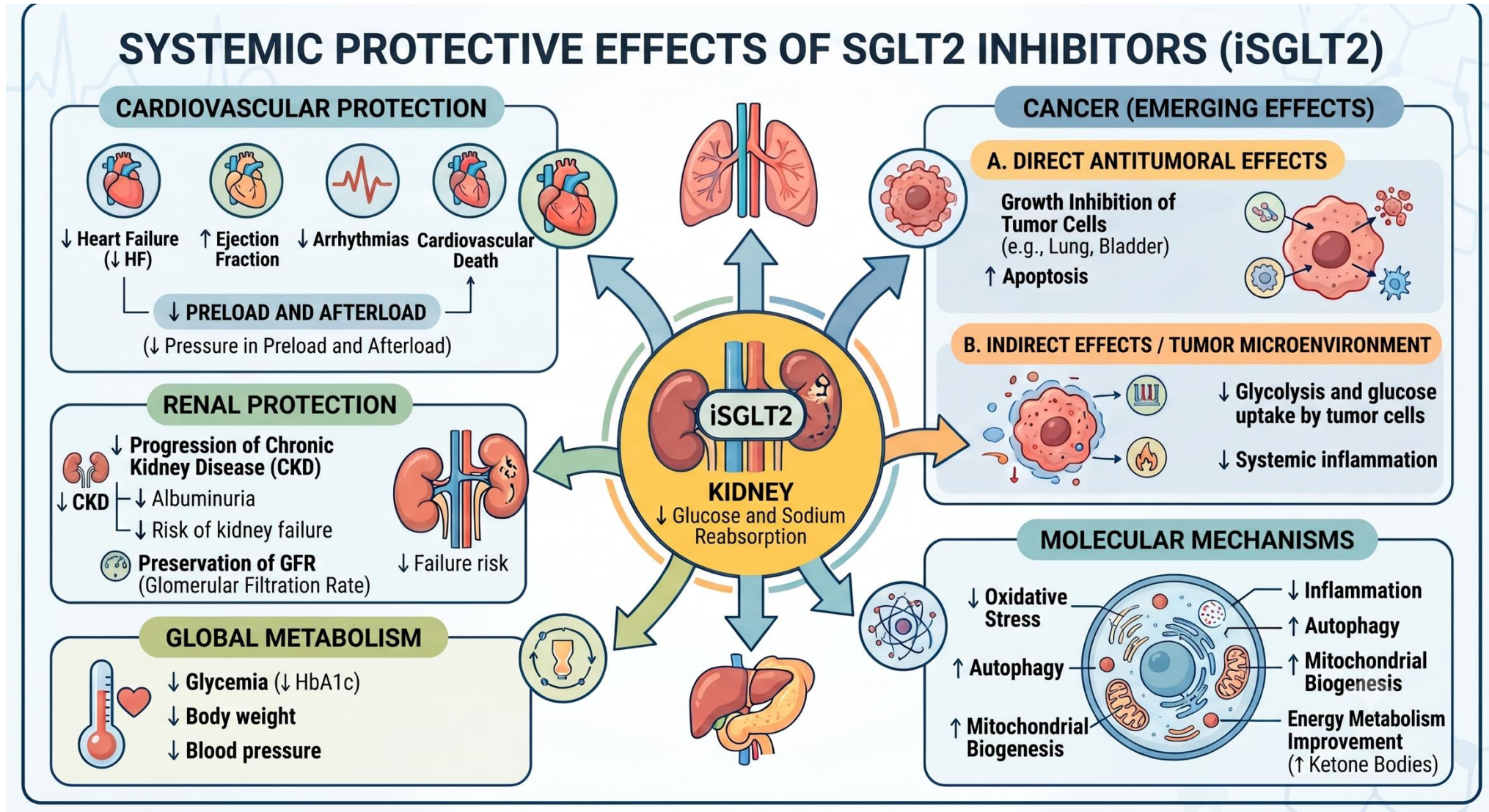
#RenalHealth



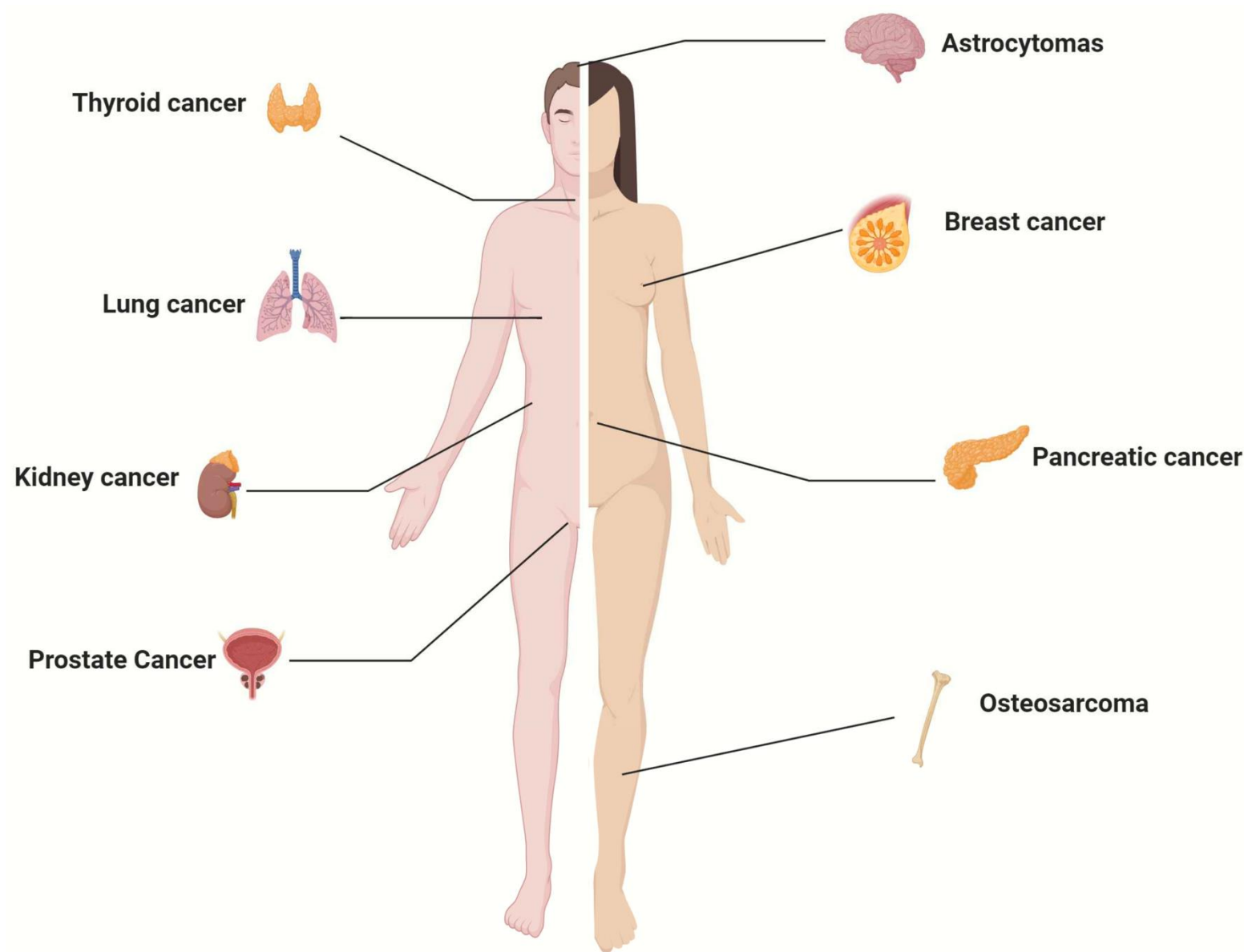
Introduction



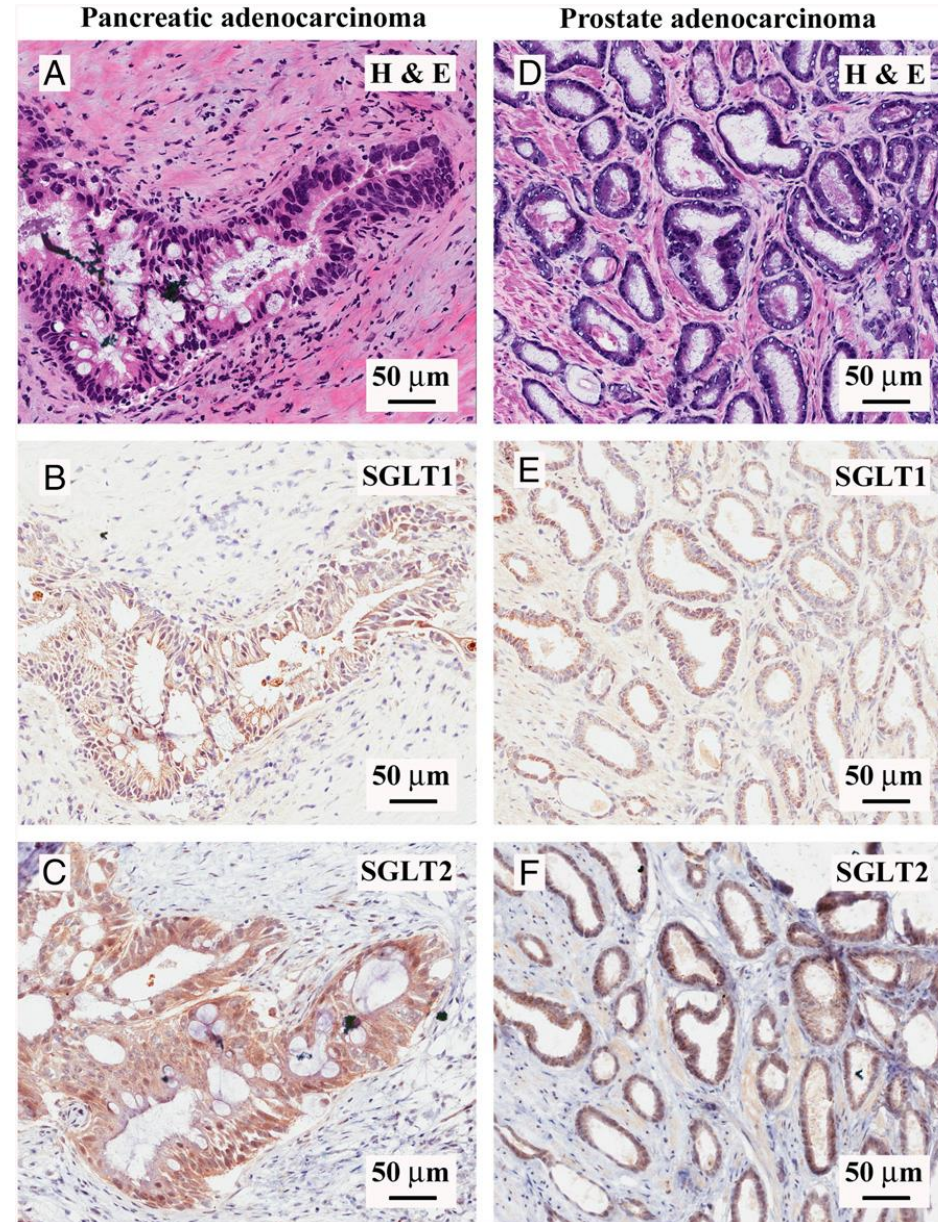
SGLT2i protective effects



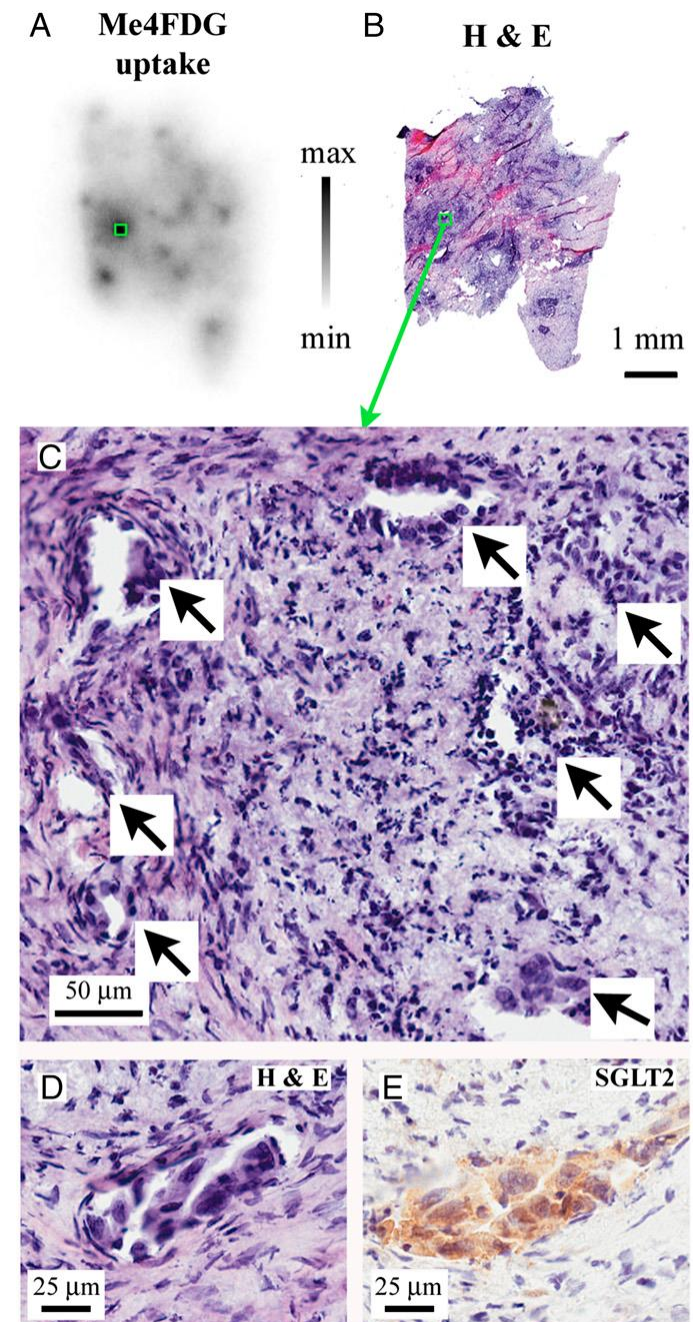
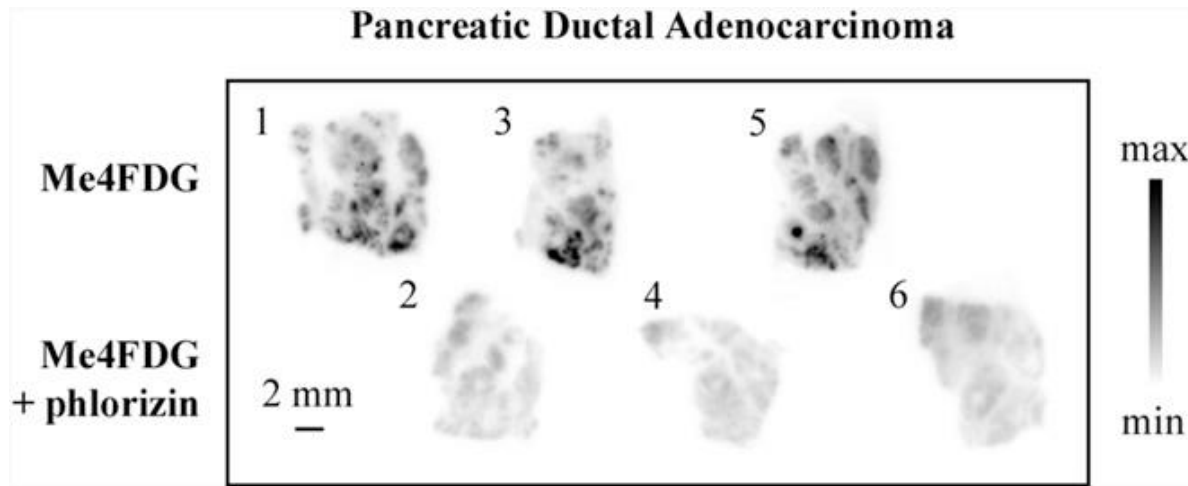
SGLT2i in cancer



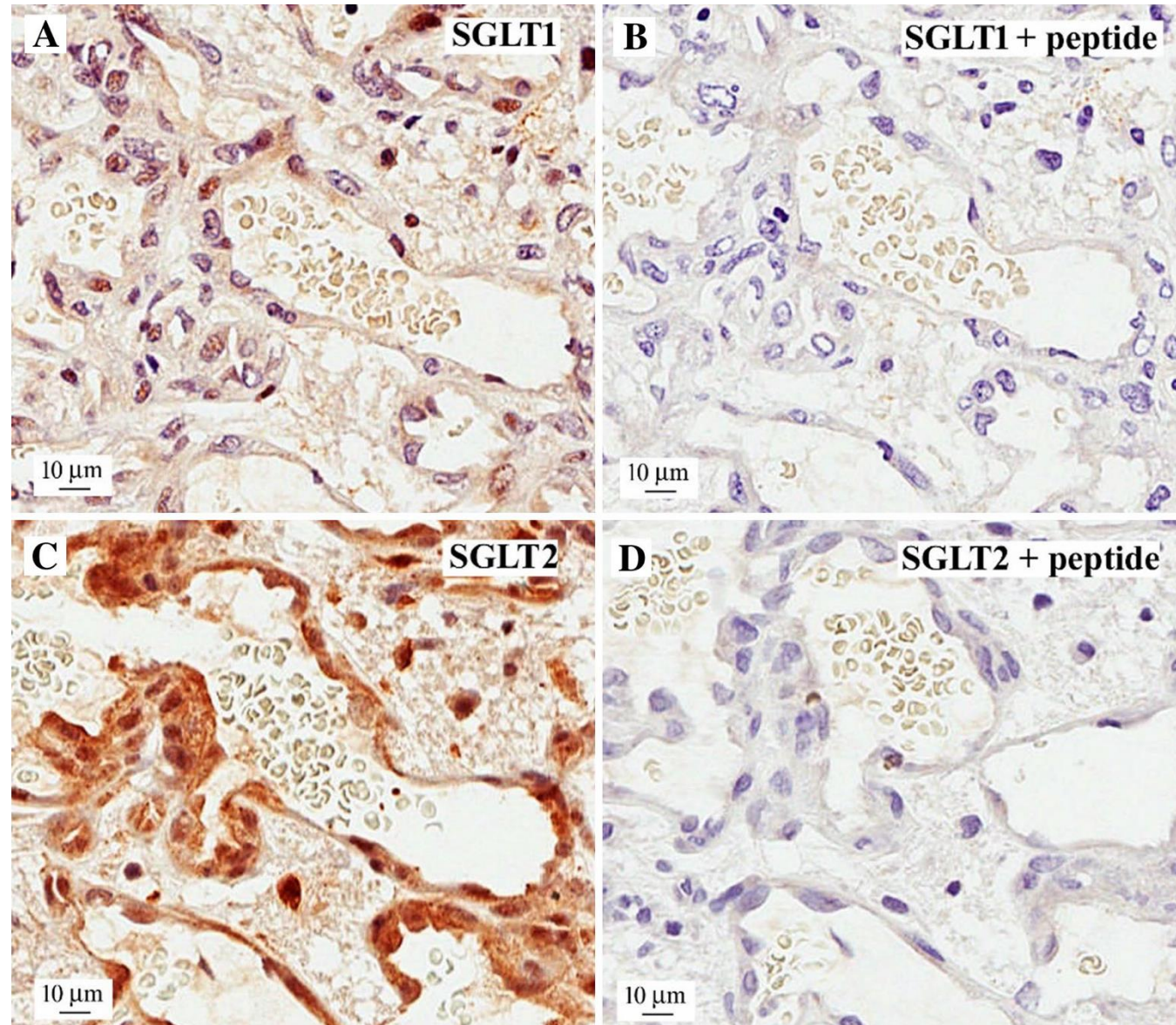
SGLT2i in cancer



SGLT2i in cancer



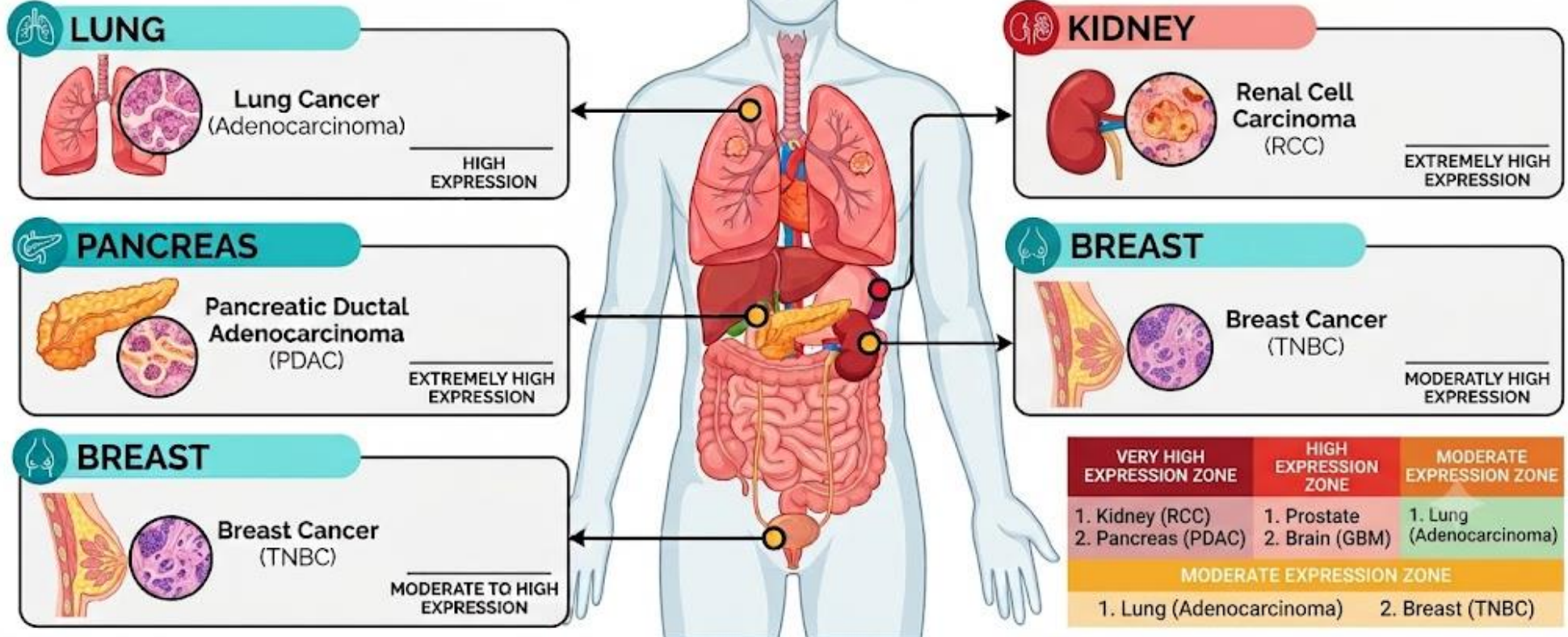
SGLT2i in cancer



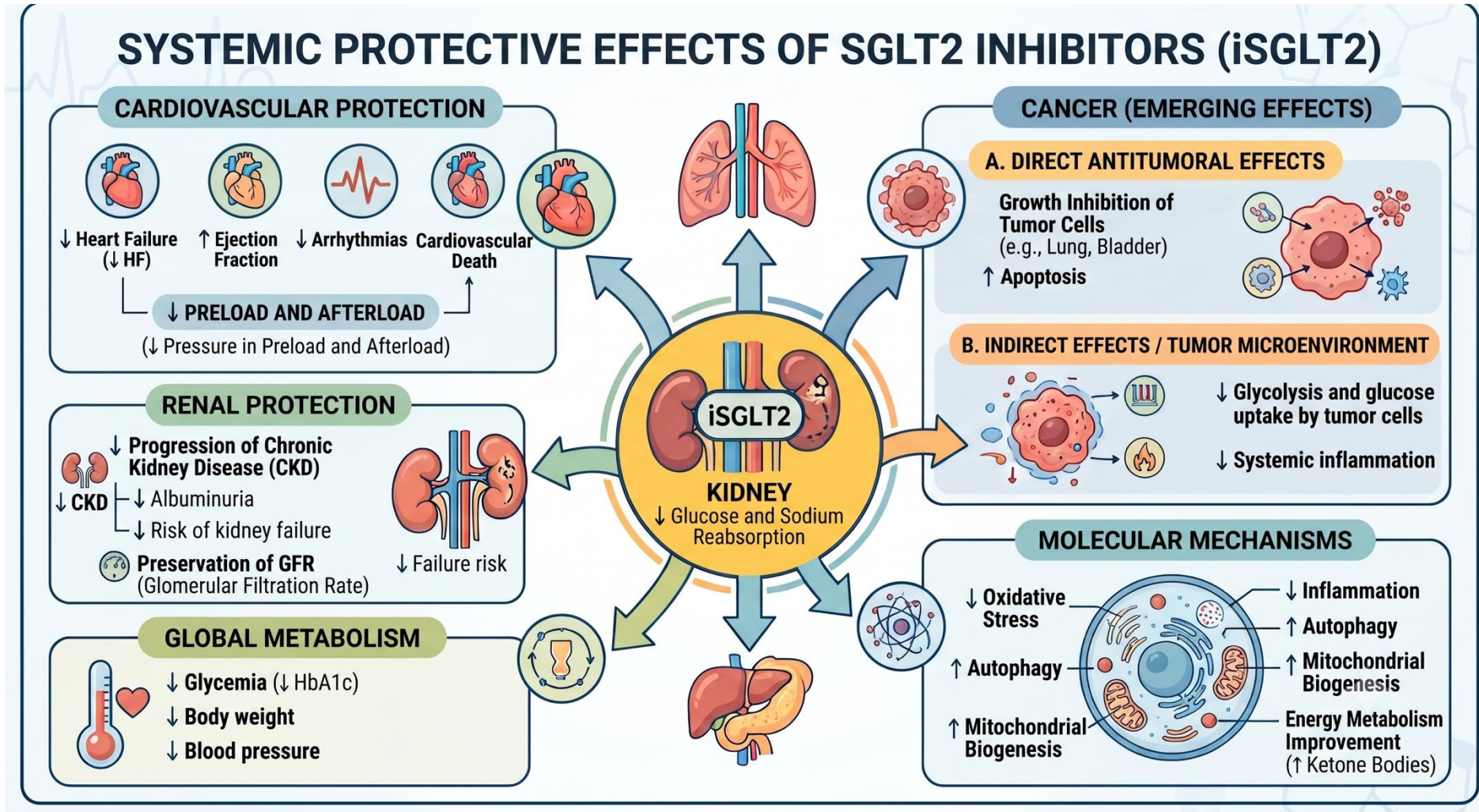
SGLT2i in cancer

TUMOR OVEREXPRESSION OF SGLT2 (ORGANIZED BY EXPRESSION LEVEL)

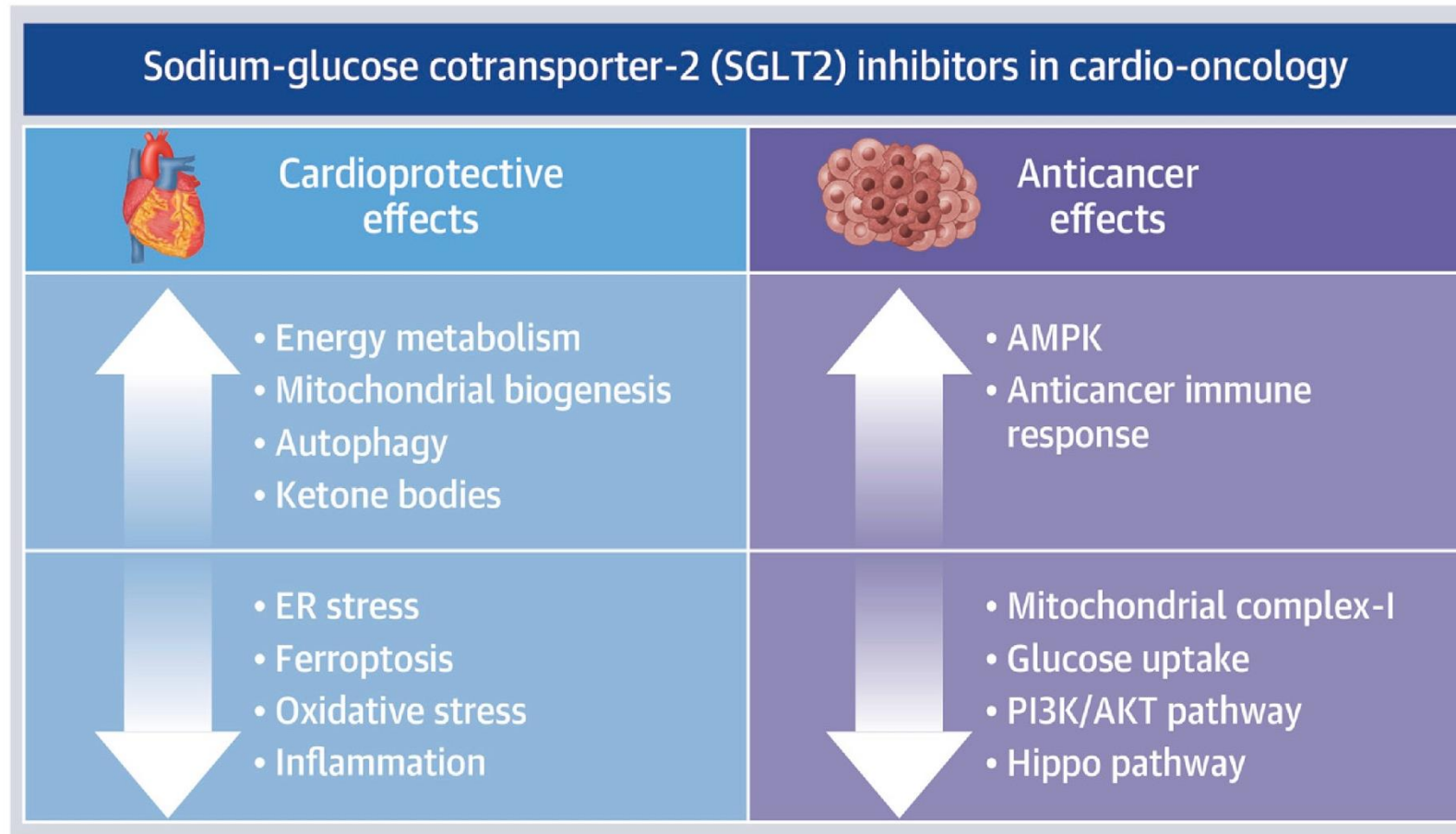
LOW  VERY HIGH EXPRESSION



Mechanisms SGLT2 & cancer

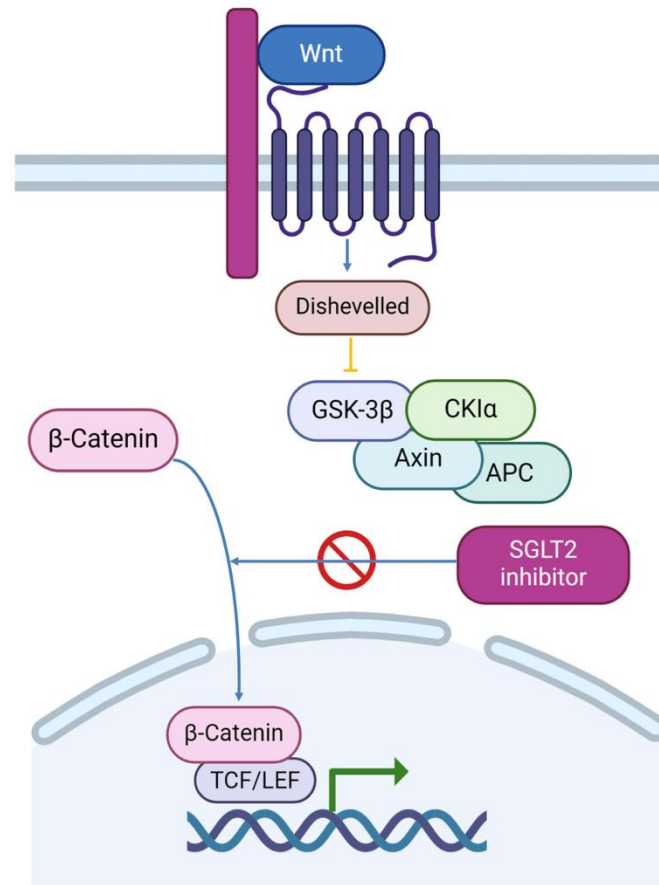


CENTRAL ILLUSTRATION: The Role of SGLT2 Inhibitors in Cardio-Oncology

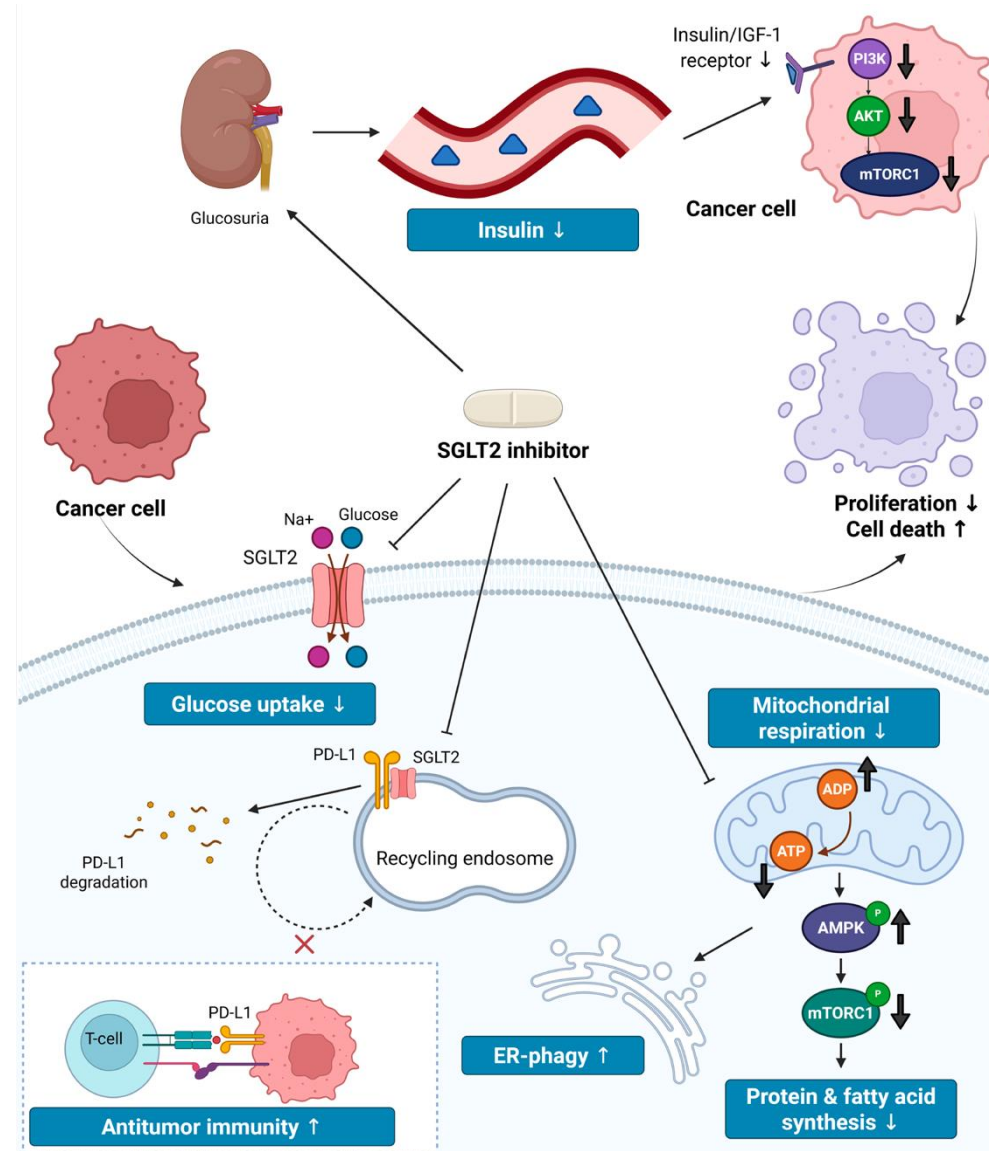


Dabour MS, et al. J Am Coll Cardiol CardioOnc. 2024;6(2):159-182.

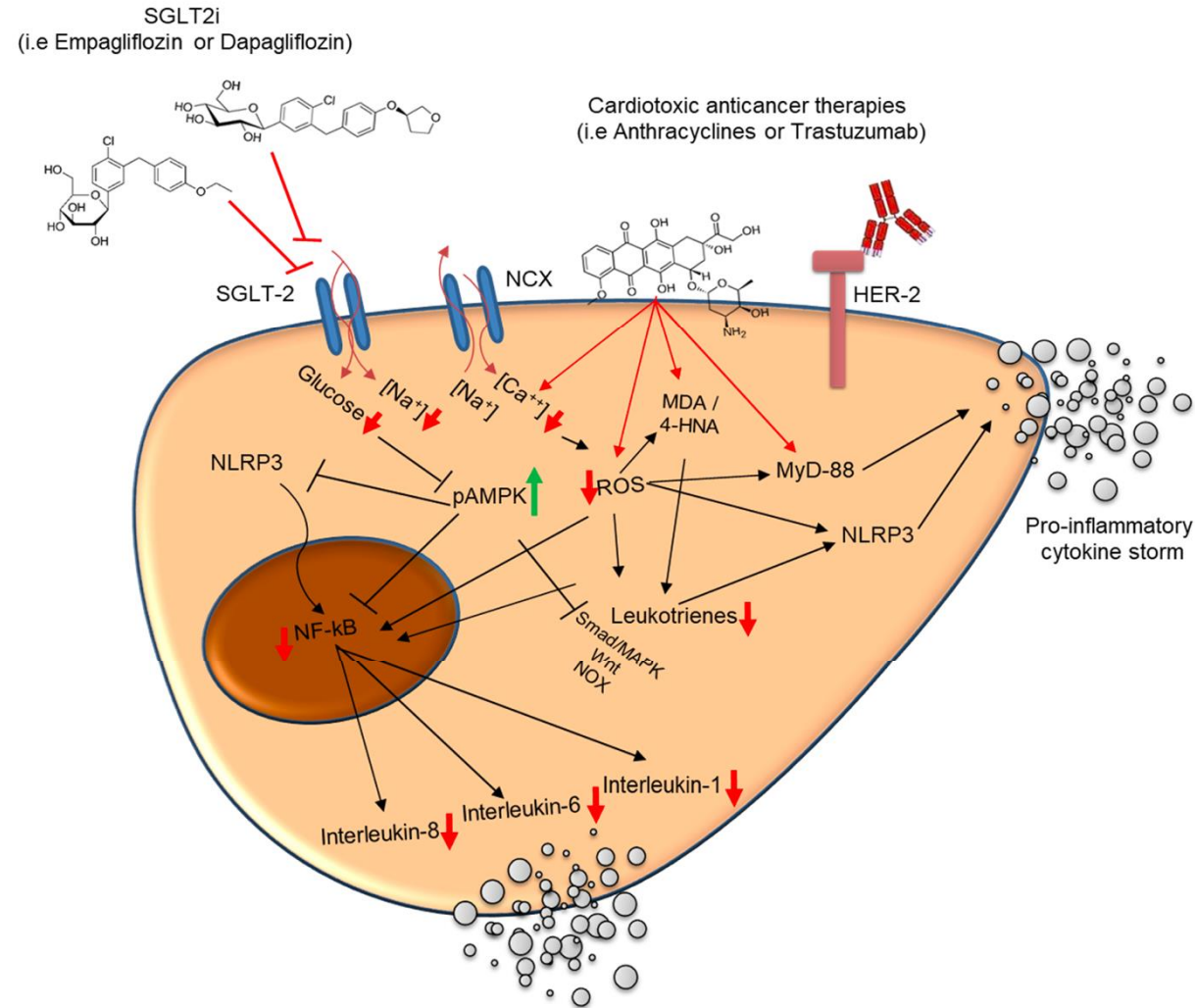
Mechanisms SGLT2 & cancer



Mechanisms SGLT2 & cancer



Mechanisms SGLT2 & cancer



SGLT2i & cancer incidence

SGLT-2 Inhibitors are Associated With a Lower Risk of Multiple Myeloma

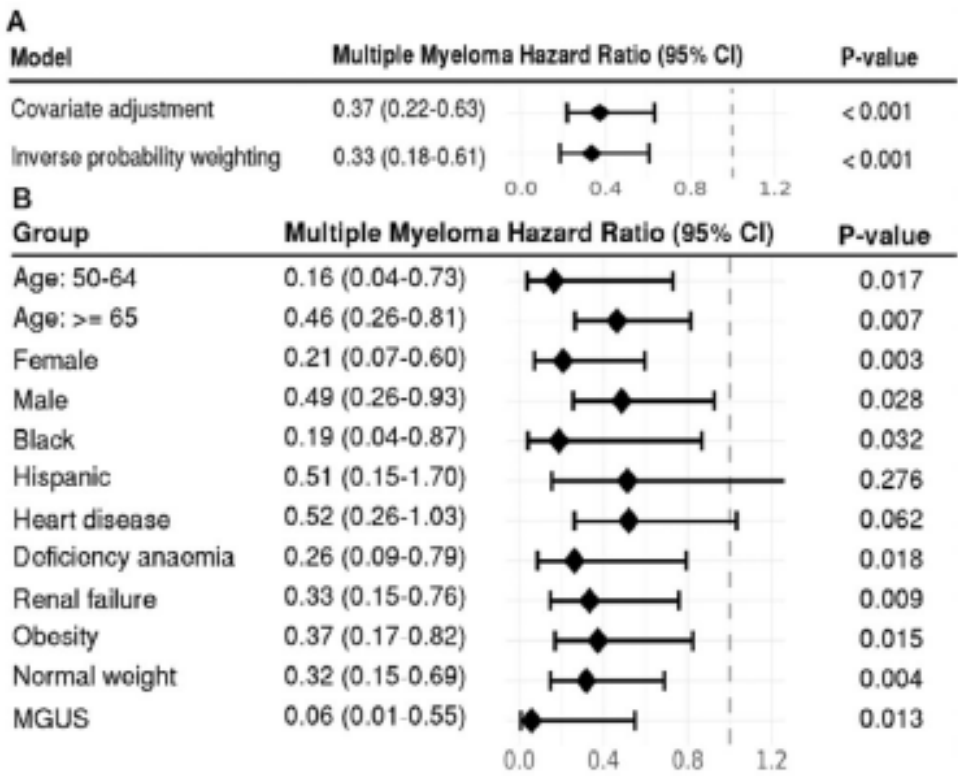
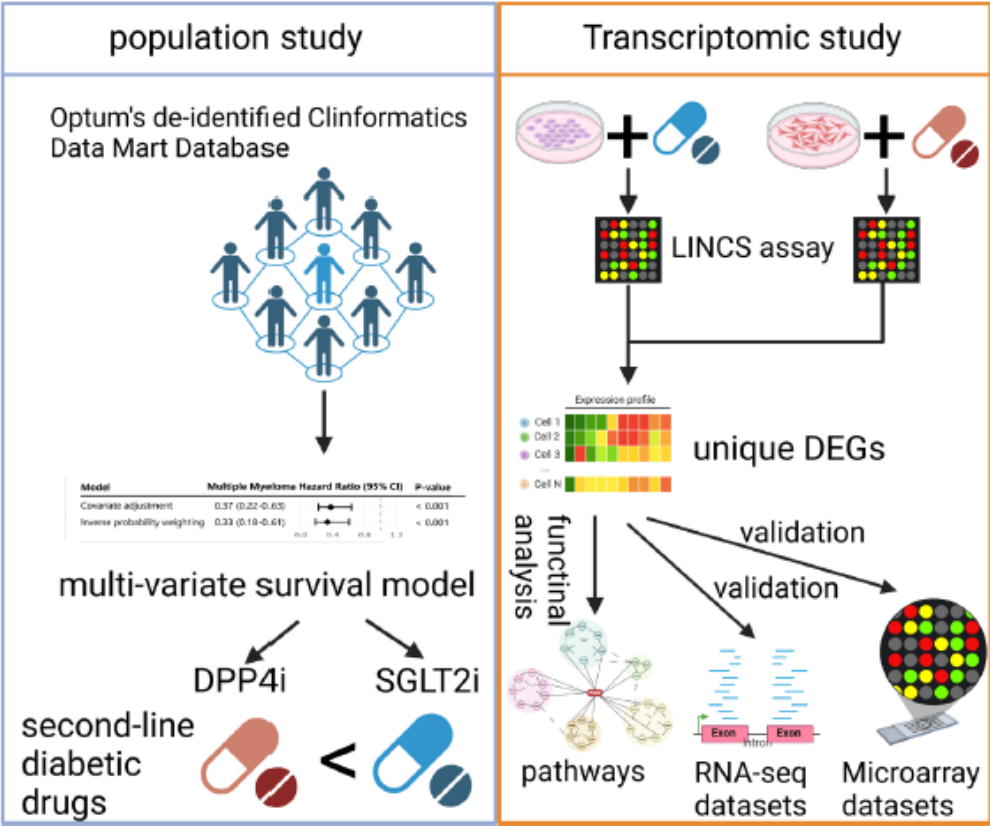


FIGURE 2 | Hazard ratios of sodium-glucose transport protein-2 inhibitors (SGLT2i) compared with dipeptidyl peptidase-4 inhibitors (DPP4i). (A) Associations with multiple myeloma in all individuals. (B) Associations with multiple myeloma in subpopulations.

SGLT2i & cancer incidence

Table 2. Incidence of Lung Cancer comparing SGLT-2 inhibitors with sulfonylureas in adults with type 2 diabetes and COPD

Reduced Risk of Lung Cancer Associated with SGLT2i

Inhibitors in Patients with COPD and Type 2 Diabetes

	4-year cumulative incidence (%)		Hazard ratio (95% CI)	
	SGLT2i	SU	Adjusted*	IPTW
Overall	46 (1.6)	188 (2.7)	0.70 (0.49-0.99)	0.73 (0.60-0.90)
Subgroup				
Age				
<65	15 (1.0)	43 (2.0)	0.62 (0.33-1.18)	0.63 (0.42-0.94)
≥65	31 (2.2)	145 (3.1)	0.71 (0.47-1.09)	0.80 (0.63-1.02)
Sex				
Male	37 (2.3)	168 (4.3)	0.64 (0.43-0.94)	0.66 (0.53-0.83)
Female	9 (0.7)	20 (0.7)	1.27 (0.52-3.11)	1.40 (0.82-2.39)
Tobacco use status				
Persons with never tobacco use	14 (1.1)	48 (1.6)	0.95 (0.49-1.83)	0.99 (0.68-1.44)
Persons with ever tobacco use	25 (2.3)	101 (4.1)	0.63 (0.39-1.02)	0.69 (0.52-0.91)
Tobacco use intensity, pack-years				
<30 pack-years	16 (1.1)	59 (1.8)	0.87 (0.47-1.61)	0.93 (0.67-1.31)
≥30 pack-years	23 (2.4)	90 (4.2)	0.64 (0.39-1.06)	0.69 (0.53-0.93)
COPD duration				
≤6-year	22 (1.6)	107 (2.7)	0.66 (0.40-1.09)	0.70 (0.53-0.93)
>6-year	24 (1.5)	81 (2.8)	0.77 (0.47-1.27)	0.77 (0.58-1.04)
History of severe COPD exacerbations in the previous year				
No	44 (1.6)	176 (2.7)	0.72 (0.50-1.04)	0.74 (0.60-0.92)
Yes	2 (0.9)	12 (2.6)	0.43 (0.08-2.34)	0.59 (0.26-0.93)
Use of ICS-containing regimens				
No	28 (1.5)	127 (2.4)	0.74 (0.47-1.15)	0.84 (0.66-1.07)
Yes	18 (1.8)	61 (4.1)	0.68 (0.38-1.20)	0.54 (0.38-0.78)
Use of metformin				
No	4 (0.6)	31 (3.0)	0.27 (0.09-0.85)	0.41 (0.22-0.75)
Yes	42 (1.7)	157 (2.7)	0.80 (0.55-1.16)	0.80 (0.64-0.99)

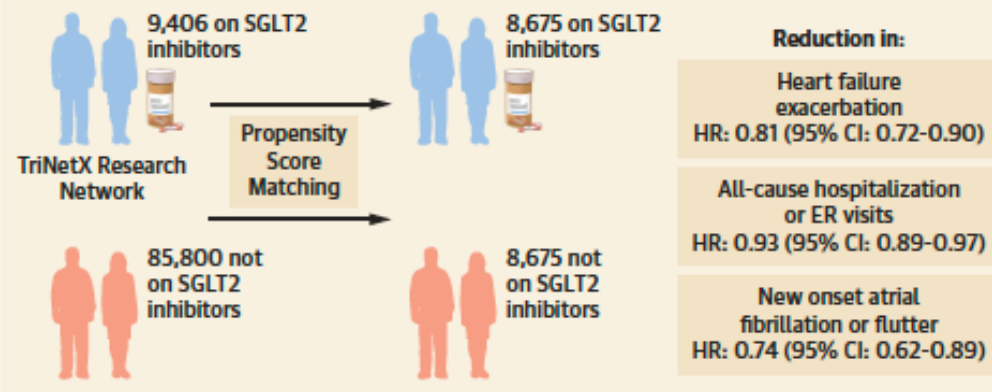
COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroid; IPTW, inverse probability of treatment weighting; SGLT2i, sodium glucose cotransporter 2 inhibitor; SU, sulfonylurea.

*Adjusted for age, sex, BMI (category), alcohol use status (yes or no), tobacco use status (ever vs. never), year at medication initiation of SGLT-2 inhibitor or sulfonylurea, COPD duration, use of ICS-containing regimens, duration of type 2 diabetes, glucose-lowering medications other than the index study drug, comorbidities (hypertension, dyslipidemia and liver cirrhosis) and Charlson Comorbidity index, and number of hospital admissions in the previous year.

SGLT2i & HF in cancer

CENTRAL ILLUSTRATION Sodium Glucose Co-Transporter 2 Inhibitors in the Prevention of Cancer Therapy-Related Cardiac Dysfunction

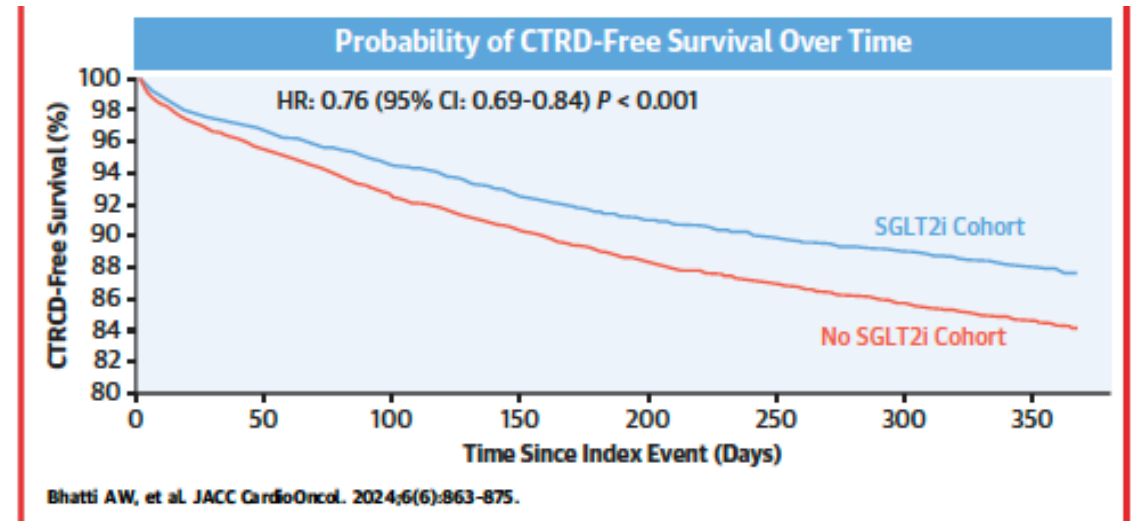
Adult Patients With Type II Diabetes and Cancer Exposed to Potentially Cardiotoxic Antineoplastic Medications



Cancer Therapy-Related Cardiac Dysfunction	HR (95% CI)
Entire Cohort	0.76 (0.69-0.84)
DRUG CLASS	
Anthracyclines	0.70 (0.58-0.85)
Monoclonal Ab	0.81 (0.66-0.98)
Proteasome Inhibitors	0.88 (0.67-1.15)
Antimetabolites	0.75 (0.65-0.86)
Alkylating Agents	0.63 (0.53-0.76)
Small Molecule TKI	0.67 (0.54-0.83)

0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1 1.2

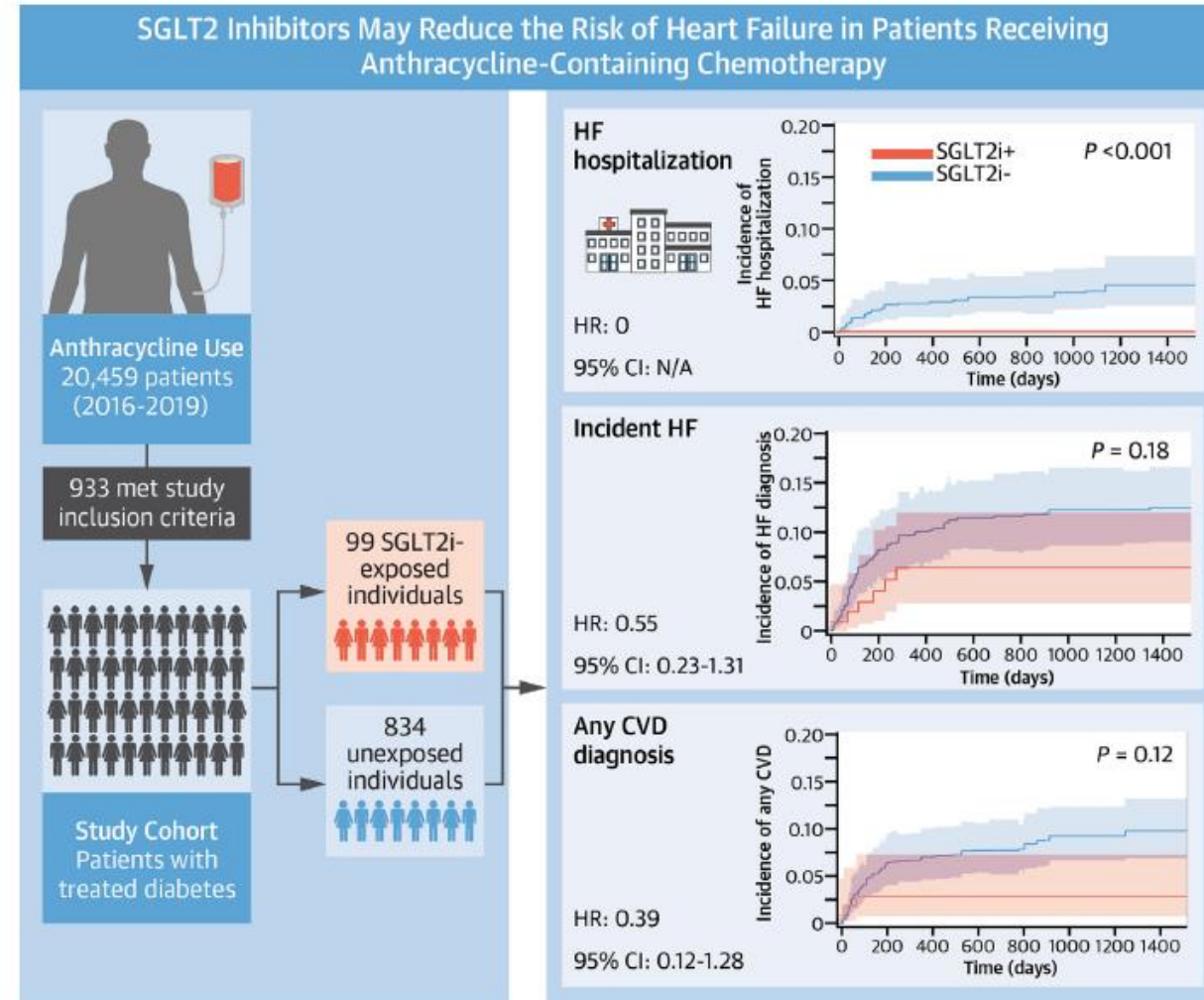
Favors SGLT2i Favors Control



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SGLT2i & HF in cancer

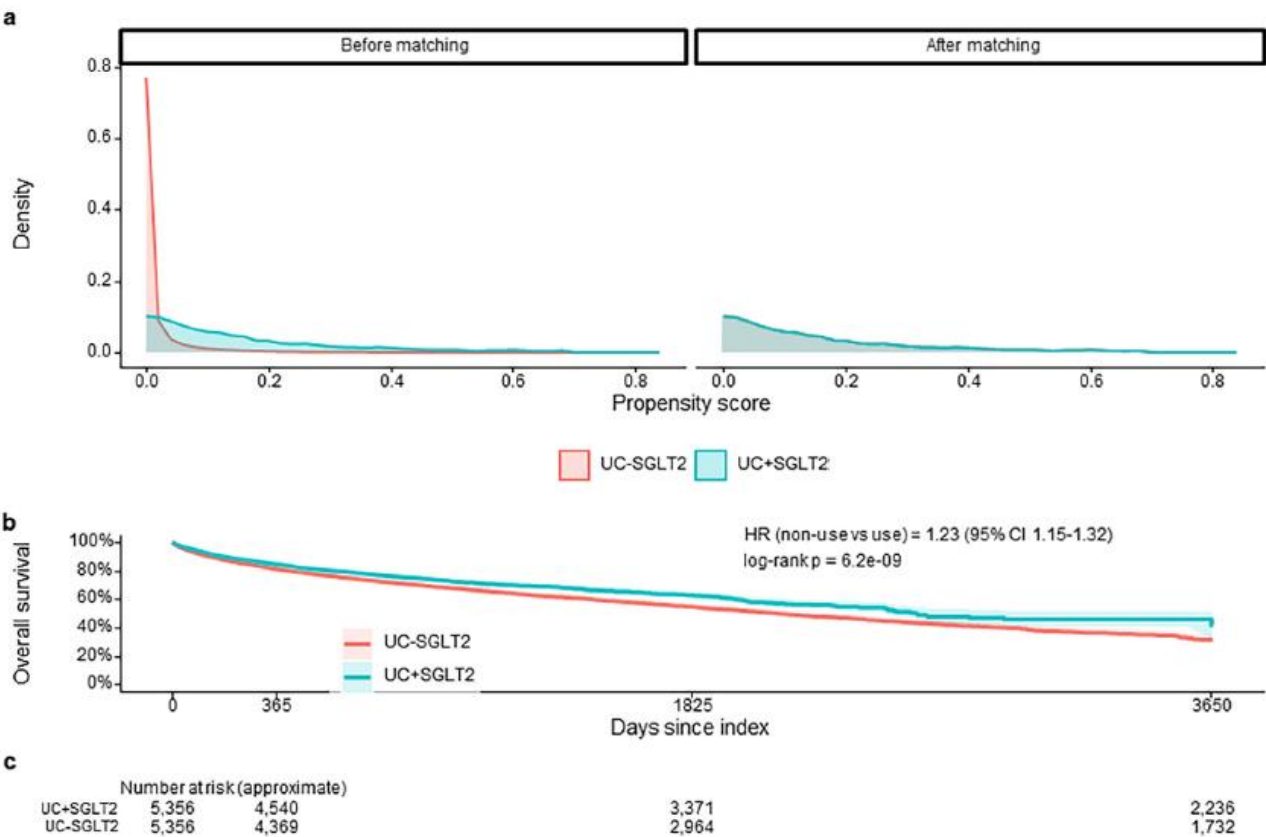
CENTRAL ILLUSTRATION The Association Between Sodium-Glucose Cotransporter 2 Inhibitors and Anthracycline Cardiotoxicity



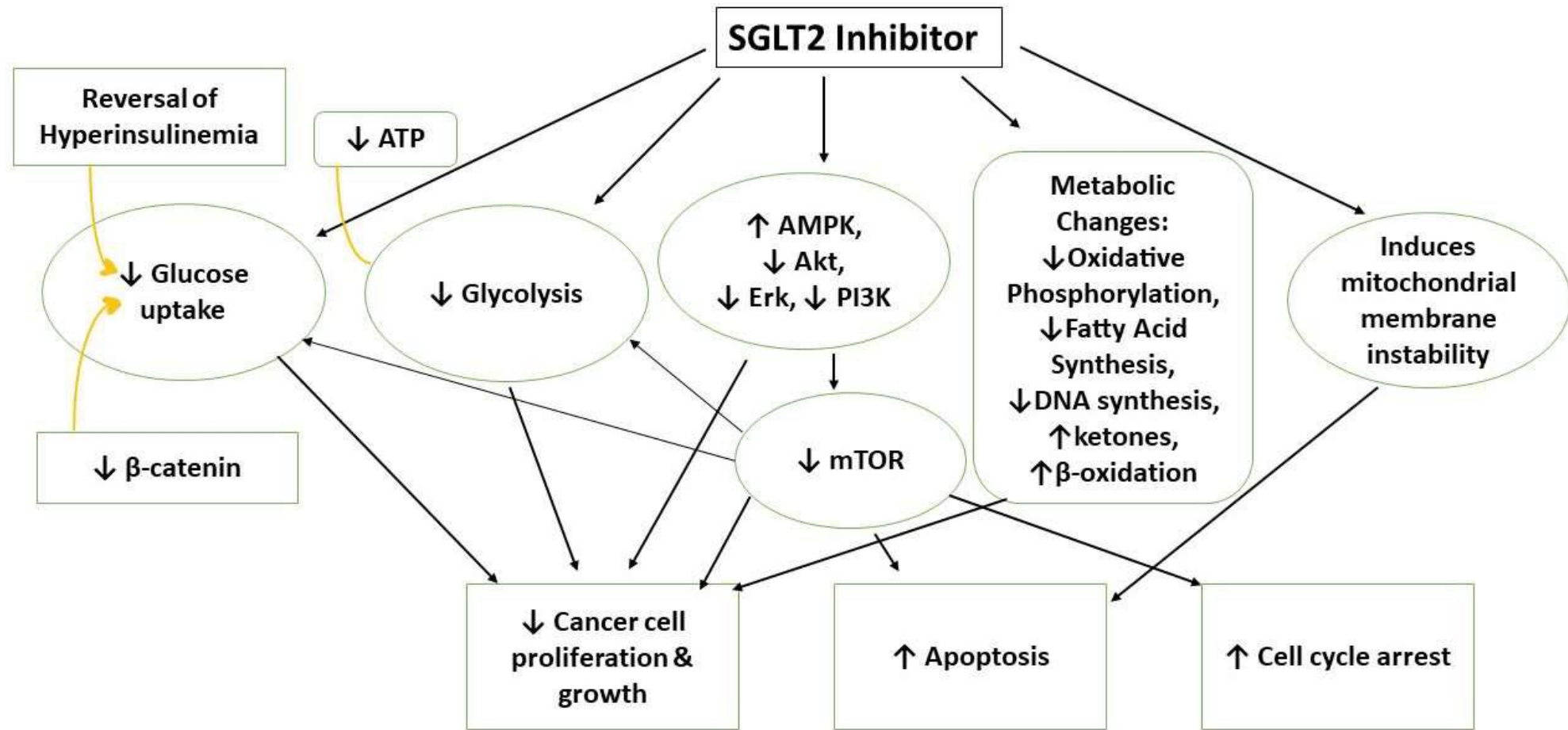
SGLT2i & Survival in cancer

96

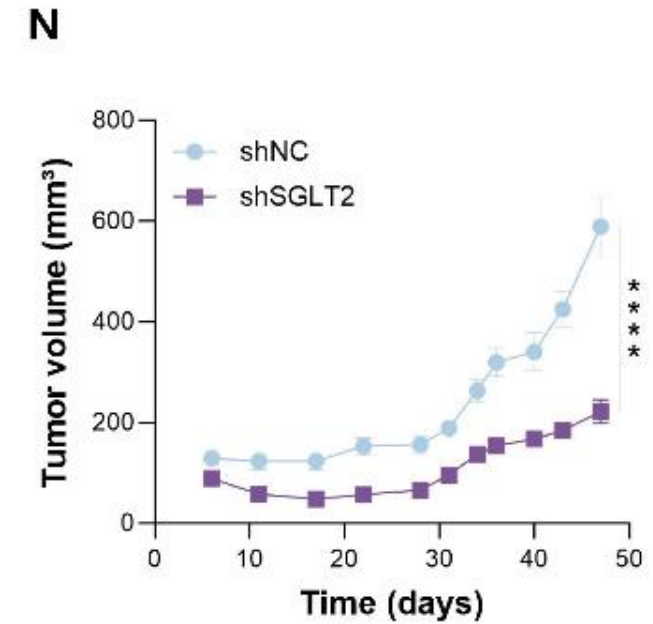
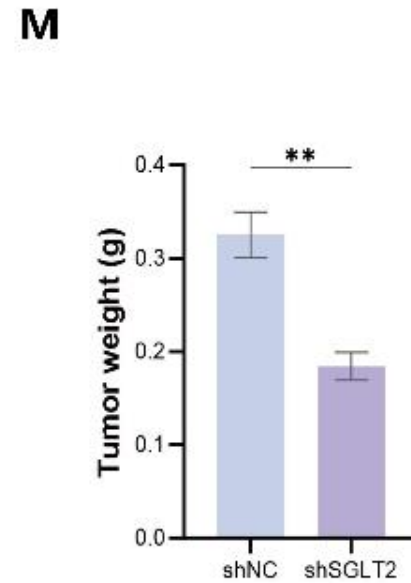
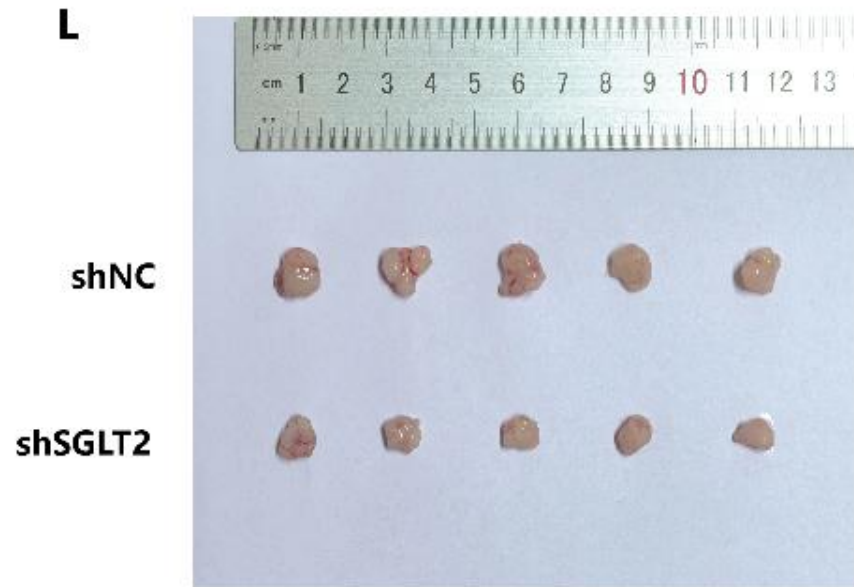
J. Kohler et al. / Urologic Oncology: Seminars and Original Investigations 44 (2026) 92–100



SGLT2i & cancer treatment



SGLT2i & cancer treatment



SGLT2i & cancer treatment toxicity

Cisplatin

CDDpress

ARTICLE OPEN

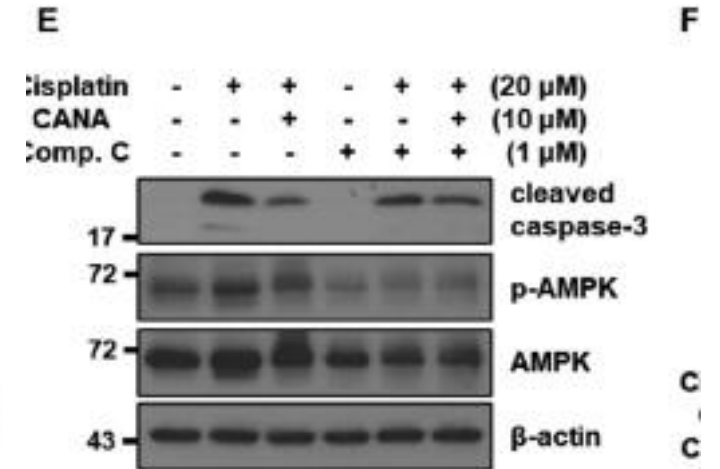
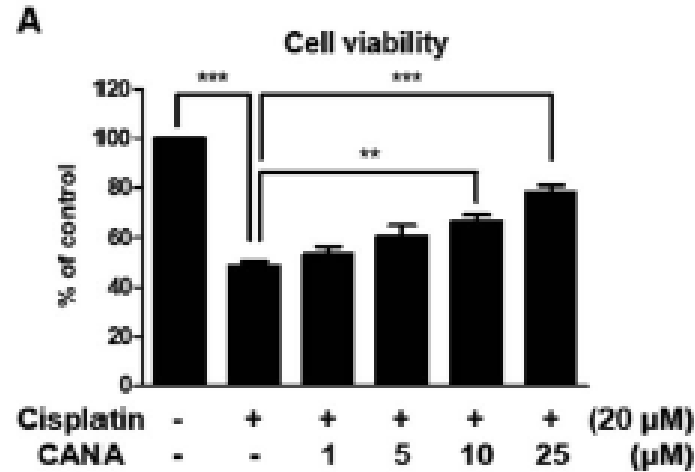
Canagliflozin protects against cisplatin-induced acute kidney injury by AMPK-mediated autophagy in renal proximal tubular cells

Cheol Ho Park^{1,2}, Bin Lee¹, Myeonggil Han¹, Woo Joong Rhee¹, Man Sup Kwak^{1,2}, Tae-Hyun Yoo^{1,2} and Jeon-Soo Shin^{1,2,4,5}

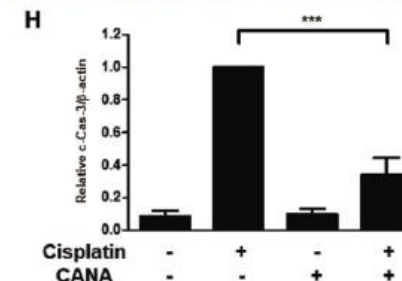
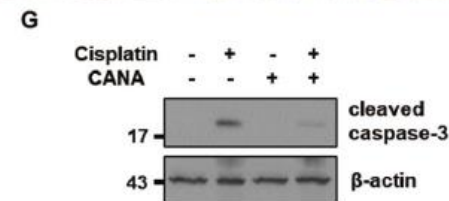
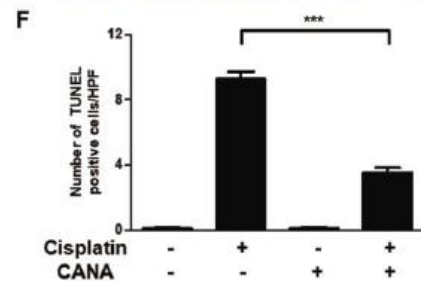
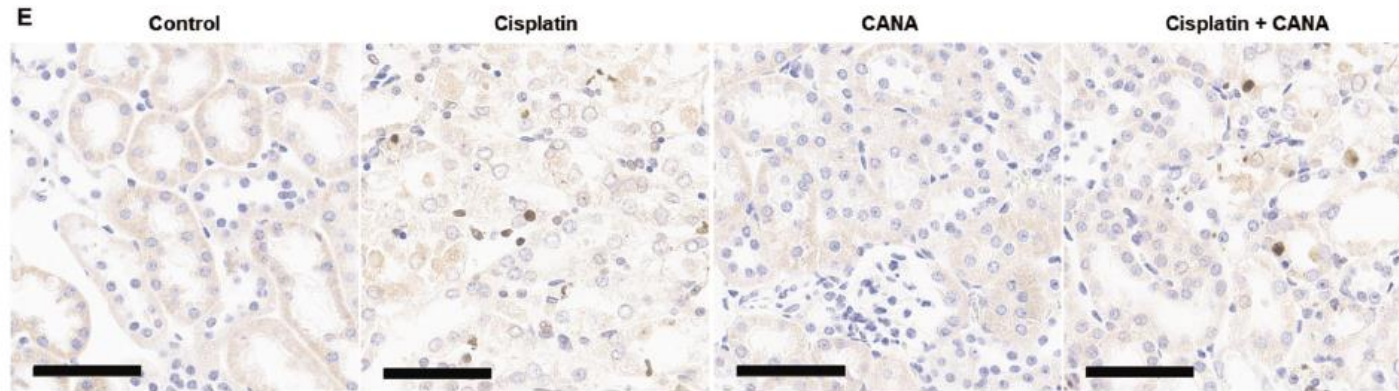
www.nature.com/cddiscovery

Check for updates

HK-2 Cells



C57BL/6 mice



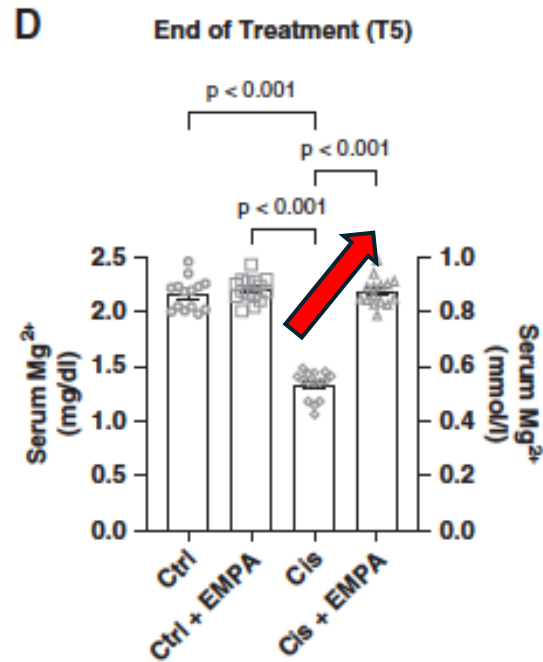
SGLT2i & cancer treatment toxicity

Basic Research

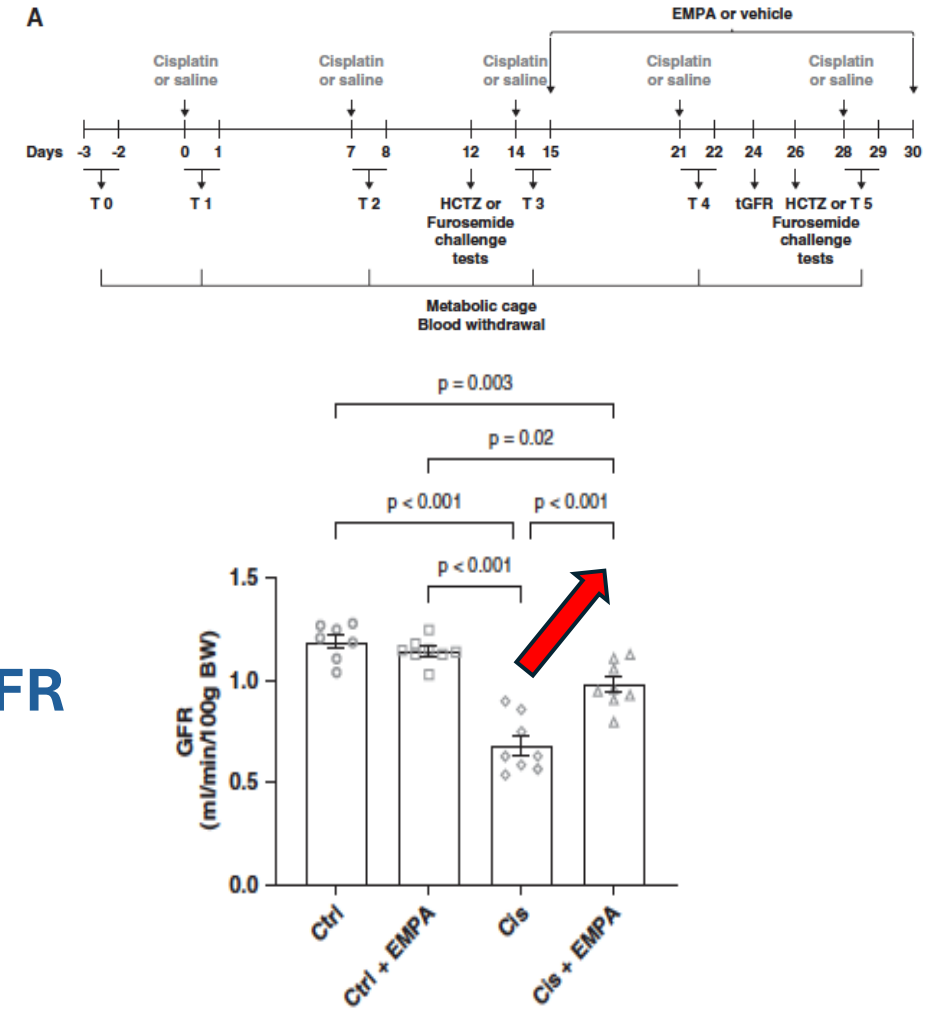
Cisplatin

SGLT2 Inhibitors Blunt Kidney Magnesium Wasting in Acute Cisplatin-Induced Hypomagnesemia with Effects on the Thick Ascending Limb and Distal Convolted Tubule

Erika F. Jesus¹, Weverton M. Luchi², Paulo C. Castro¹, Flavia L. Martins¹, Marcos V. Caetano¹, Vanderlene L. Kung³, Antonio C. Seguro⁴, James A. McCormick⁵, and Adriana C.C. Girardi¹



GFR



SGLT2i & cancer treatment toxicity

Cisplatin

KI REPORTS
KIReports.org

CLINICAL RESEARCH

Potential Benefit of Sodium-Glucose Cotransporter 2-Inhibitors in Cisplatin-Associated Nephrotoxicity Among Patients With Cancer Having Diabetes Mellitus

 Check for update

Juan J. Cintrón-García^{1,2,3,7}, Maulinkumar Patel^{4,7}, Clark R. Andersen⁵, Valda Page¹, Biruh Workeneh¹, Sreedhar Mandayam¹, Reem Al-Dallal⁶, Ala Abudayyeh¹ and Omar Mamlouk¹

Table 1. Characteristics of patients with cancer having diabetes mellitus receiving cisplatin therapy, by SGLT2i status

	Before PSM			After PSM		
	SGLT2i exposure group (n = 144)	Control group (n = 373)	SMD	SGLT2i exposure group (n = 144)	Control group (n = 144)	SMD
Patient demographics						
Age (yrs), mean (SD)	62.5 (9.68)	61.4 (10.8)	−0.12	62.5 (9.68)	63.3 (9.92)	0.08
White race	105 (72.9%)	250 (67%)	−0.13	105 (72.9%)	105 (72.9%)	0
Male sex	107 (74.3)	204 (54.7)	0.42	107 (74.3)	99 (68.8)	0.12
BSA, m ² , mean (SD)	2.08 (0.29)	2.05 (0.31)	−0.10	2.08 (0.29)	2.05 (0.29)	−0.10
Co-morbidities						
Hypertension	112 (77.8)	287 (76.9)	−0.02	112 (77.8)	110 (76.4)	−0.03
COPD	8 (5.6)	18 (4.8)	−0.03	8 (5.6)	7 (4.9)	−0.03
Liver disease	22 (15.3)	46 (12.3)	−0.09	22 (15.3)	21 (14.6)	−0.02
CHF	8 (5.6)	15 (4.0)	−0.07	8 (5.6)	8 (5.6)	0
CKD	7 (4.9)	29 (7.8)	0.12	7 (4.9)	9 (6.3)	0.06
Type of cancer			0.15			0.05
SCC	50 (34.7)	124 (33.2)		50 (34.7)	49 (34)	
Genitourinary	18 (12.5)	57 (15.3)		18 (12.5)	18 (12.5)	
Hepatobiliary	29 (20.1)	33 (8.8)		29 (20.1)	23 (16)	
Endometrial	13 (9.0)	33 (8.8)		13 (9.0)	17 (11.8)	
Lung	9 (6.3)	25 (6.7)		9 (6.3)	11 (7.6)	
Other	25 (17.4)	101 (27.1)		25 (17.4)	26 (18.1)	

SGLT2i & cancer treatment toxicity

Cisplatin

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CLINICAL RESEARCH

Potential Benefit of Sodium-Glucose Cotransporter 2-Inhibitors in Cisplatin-Associated Nephrotoxicity Among Patients With Cancer Having Diabetes Mellitus

Check for update

Juan J. Cintrón-García^{1,2,3,7}, Maulinkumar Patel^{4,7}, Clark R. Andersen⁵, Valda Page¹, Biruh Workeneh¹, Sreedhar Mandayam¹, Reem Al-Dallal⁶, Ala Abudayyeh¹ and Omar Mamlouk¹

↓ 58% AKI
↓ 77% HypoMg++
↓ 79% Anemia

Table 2. Comparison of outcomes in patients with cancer having diabetes receiving cisplatin therapy by SGLT2i status

Outcomes	SGLT2i group (n = 144)	Control group (n = 144)	Effect estimate (95% CI) ^a	P-value
AKI	20 (13.9)	41 (28.5)	0.42 (0.23–0.76)	0.004
Genitourinary infections	13 (9.0)	17 (11.8)	0.77 (0.36–1.67)	0.51
Hyponatremia	87 (60.4)	97 (67.4)	0.73 (0.45–1.18)	0.20
Hypomagnesemia	33 (23.2)	82 (57.3)	0.23 (0.14–0.38)	< 0.001
Anemia	120 (83.3)	137 (95.1)	0.21 (0.09–0.52)	< 0.001
eGFR at 3 mos, mean (SD) (ml/min per 1.73 m ²)	84.4 (25.7)	78.3 (25.1)	6.08 (0.23–11.93)	0.043

AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; CI, confidence interval; SGLT2i, sodium-glucose cotransporter-2 inhibitors.

^aEffect estimates are odds ratios (ORs) for binary outcomes and mean differences (MDs) for continuous outcomes, with 95% CIs.

All data are expressed as number of patients (%) unless otherwise indicated.

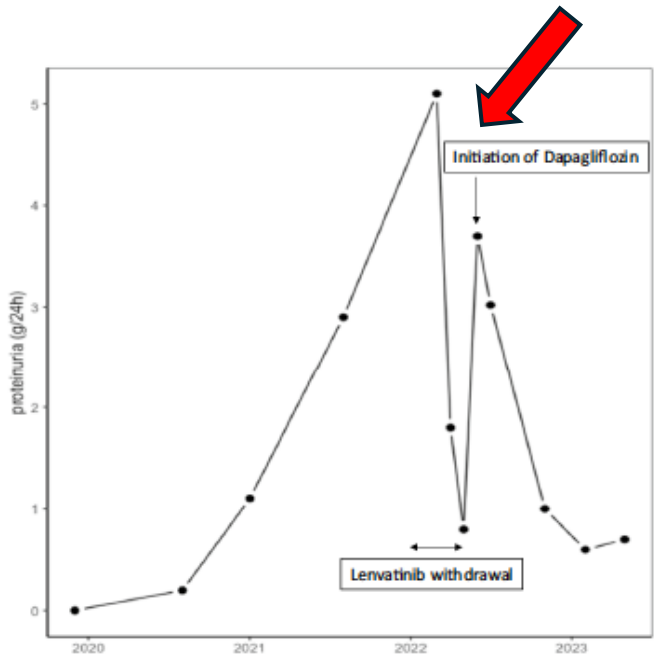
SGLT2i & cancer treatment toxicity

TKI. Dapa Proteinuria

Table 1 Patient's characteristics at baseline (before SGLT2i)

Characteristics at baseline	
Age (years)	66
Systolic blood pressure (mmHg)	140
Diastolic blood pressure (mmHg)	80
BMI (kg/m ²)	20
Creatininemia (mg/dL)	0.5
eGFR (mL/min/1.73m ²)	99
eGFR category	G1
Albuminuria (g/g)	2.5
Albuminuria category	A3

BMI body mass index, *eGFR* estimated glomerular filtration rate (according to CKD-Epi equation); eGFR and albuminuria categories are described according to KDIGO Guidelines[5]



Conclusions

- SGLT2i **cardio-renal protection** and promising strategy **cancer-associated nephrotoxicity** in onco-nephrology.
- SGLT2 is **overexpressed** in various solid tumors, and may serve as target for disrupting cancer cell glucose uptake and metabolism.
- SGLT2i reduce overall **cancer incidence** and **mitigate cardiotoxicity** from antineoplastic therapies.

Conclusions

- SGLT2i has potential benefits in reducing **cisplatin-induced and tyrosine kinase inhibitor (TKI)-associated nephrotoxicity**.
- Ongoing research continues to map their complex molecular mechanisms to optimize their dual cardio-renal and antitumoral benefits.

Thank you!!



pepasolerr



@PepaSolerR

