Rene e Diabete

SGLT2i: oltre HF e CKD

Anna Solini

Università di Pisa

Disclosures

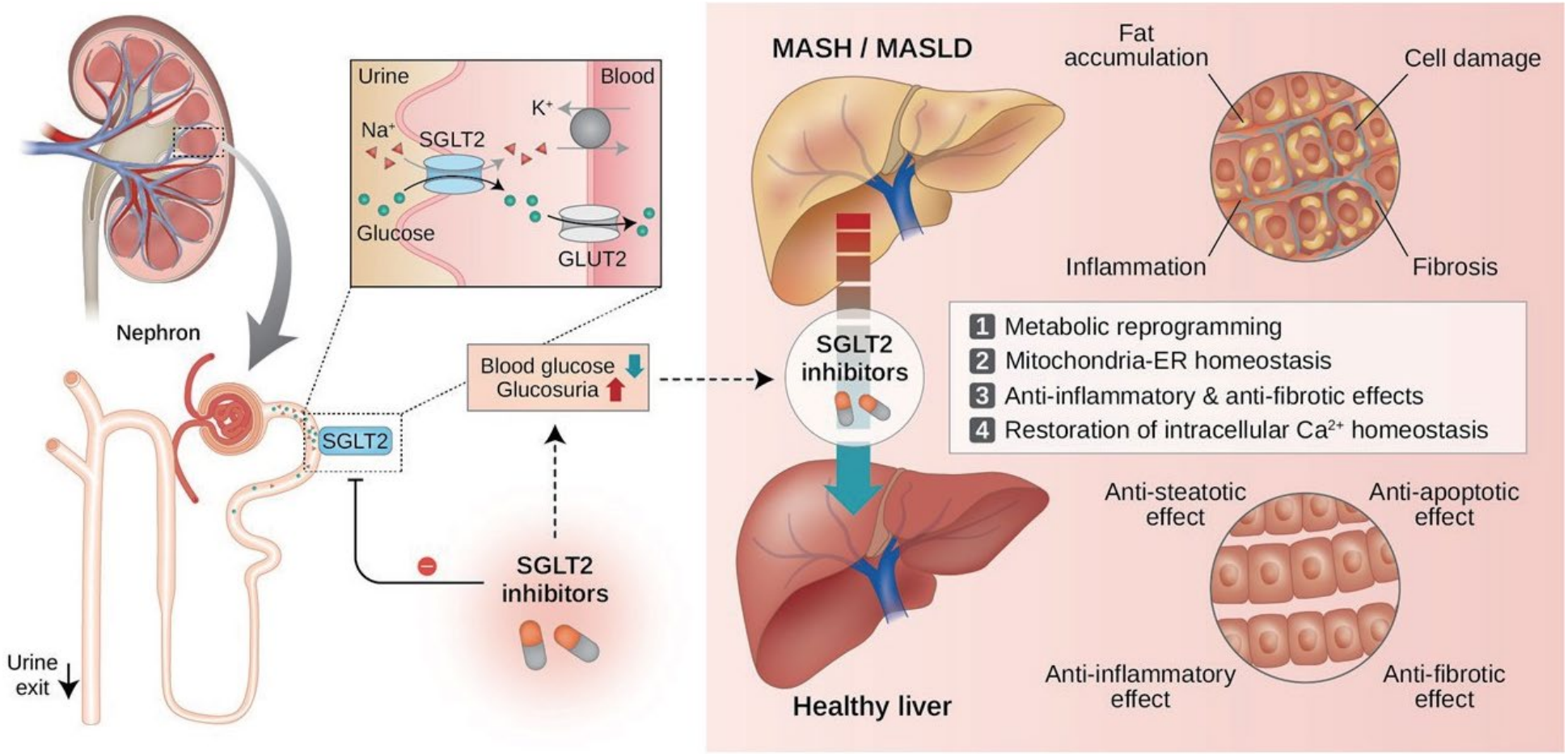
Advisory Board: Sankyo

Speaker Bureau: Astra Zeneca, Lilly, Novo, sanofi

Agenda

- ✓ MASLD
- ✓ Neurodegenerative diseases
- ✓ Respiratory disease outcomes
- ✓ Relevant clinical implications of the anti-inflammatory effect

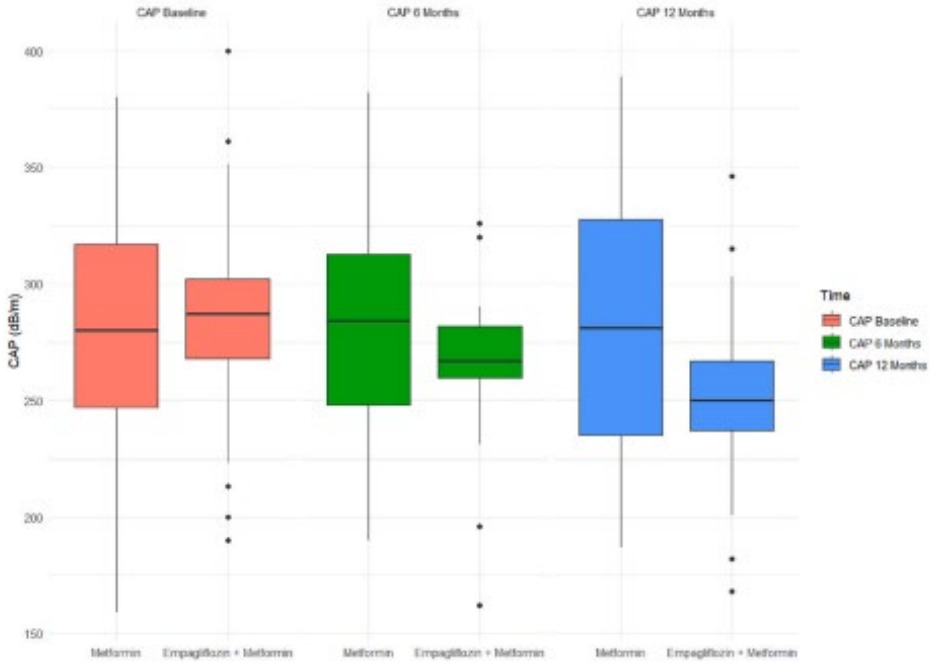
SGLT2 Inhibition Drives Systemic Metabolic Reprogramming and Hepatoprotection in MASLD



Noh SW, Endocrinol Metab 2025

Empagliflozin as Add-On to Metformin on MASLD Progression in T2D: The IMAGIN Study

Box plot analysis of CAP variation in metformin and combination groups



Univariable and multivariable logistic regression model for steatosis amelioration among the study population

Baseline Variables	Univariable Analysis				Multivariable Analysis			
	OR	95 % CI		P	OR	95 % CI		P
Age	0.96	0.92	1.01	*0.055*				
Sex								
M (ref)	1							
F	0.73	0.31	1.72	*0.477*				
Hypertension	0.87	0.35	2.16	*0.757*				
Diabetes duration	1.03	0.90	1.18	*0.668*				
Diabetes familiarity	2.89	0.57	14.68	*0.201*				
ACEi	0.31	0.11	0.89	***0.030***	0.36	0.11	1.21	0.097
ARB	0.62	0.23	1.69	*0.349*				
Diuretics	0.54	0.17	1.77	*0.540*				
Beta-blockers	0.80	0.29	2.20	*0.672*				
Alfa-blockers	1.40	0.12	16.04	*0.787*				
Ca antagonists	0.12	0.01	1.09	*0.059*				
Statins	1.58	0.67	3.71	*0.297*				
Antiaggregants	1.67	0.39	7.21	*0.494*				
Combination therapy	10.29	3.60	29.44	***<0.001***	9.79	3.37	28.49	**<0.001**
BMI	0.99	0.90	1.09	*0.883*				
$HbA1_c$	1.37	0.98	1.80	*0.080*				
Glucose	0.96	0.91	1.01	*0.098*				
AST	1.01	0.98	1.03	*0.609*				
ALT	1.01	0.99	1.02	*0.169*				
Platlets	1.01	1.00	1.02	*0.266*				
Albumin	0.85	0.27	2.71	*0.790*				
eGFR	0.98	0.94	1.03	*0.455*				
Uric acid	1.77	0.67	4.65	*0.247*				

ACEi angiotensin converting enzyme inhibitor; ARB angiotensin receptor blocker; Ca calcium; BMI body mass index; $HbA1_c$ glycated haemoglobin; AST aspartate aminotransferase; ALT alanine aminotransferase; CAP controlled attenuated parameter; eGFR estimated glomerular filtration rate.

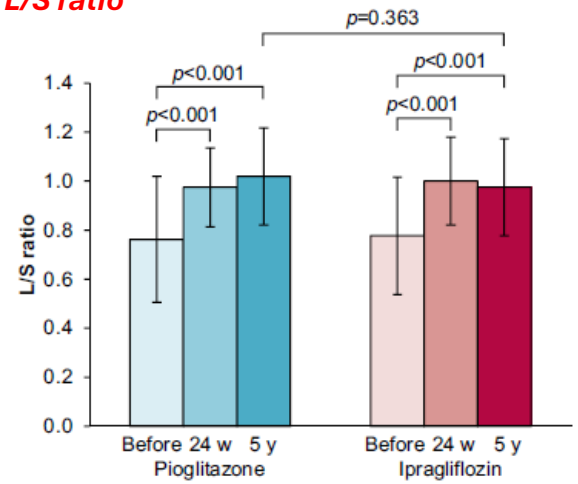
Caturano A, NMCD 2026

Effect of Ipragliflozin in MASLD

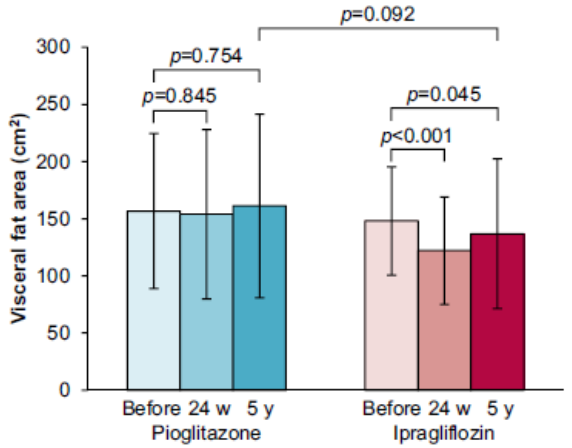
5 year observational follow-up of a randomized, 24 week, active controlled trial

Changes from baseline

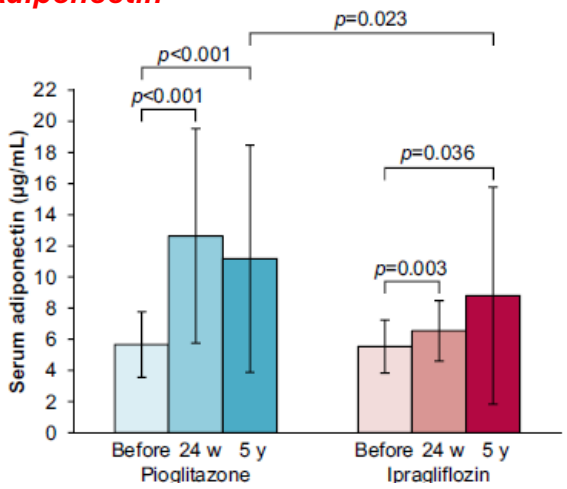
L/S ratio



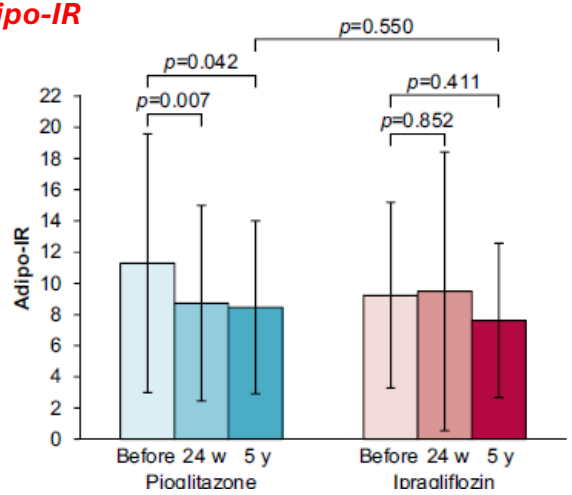
Abdominal VFA



Adiponectin



Adipo-IR

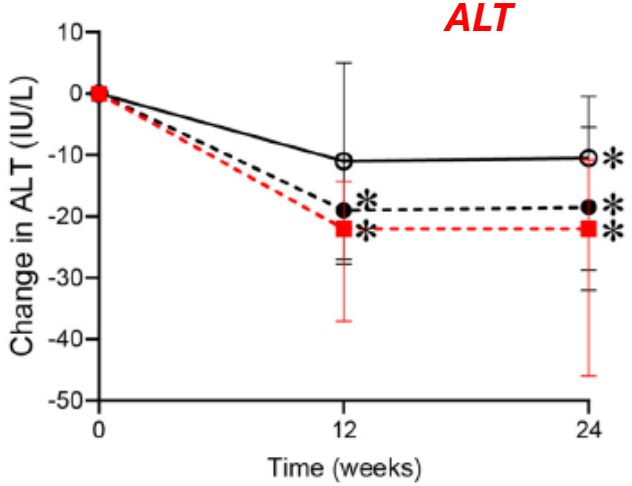


L/S ratio, liver-to-spleen attenuation ratio
Adipo-IR, adipose tissue insulin resistance

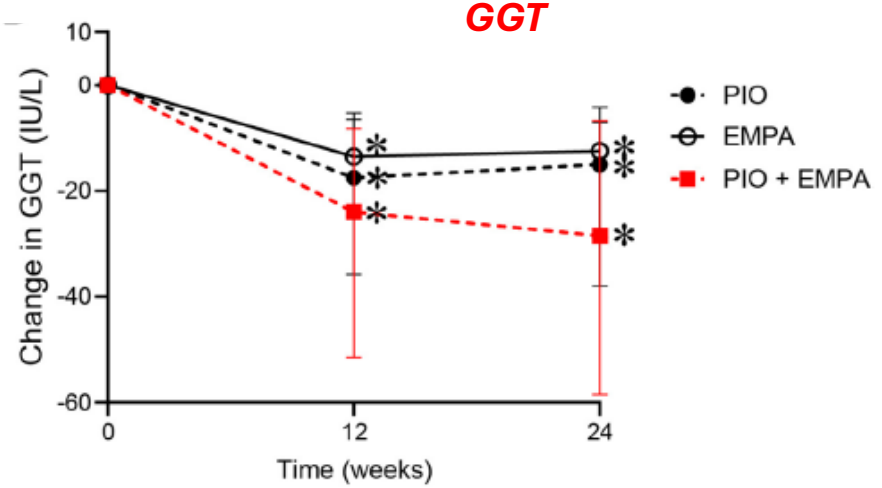
Ito D, J Diabetes Investig 2024

Synergistic Benefit of Thiazolidinedione and SGLT2i for MASLD

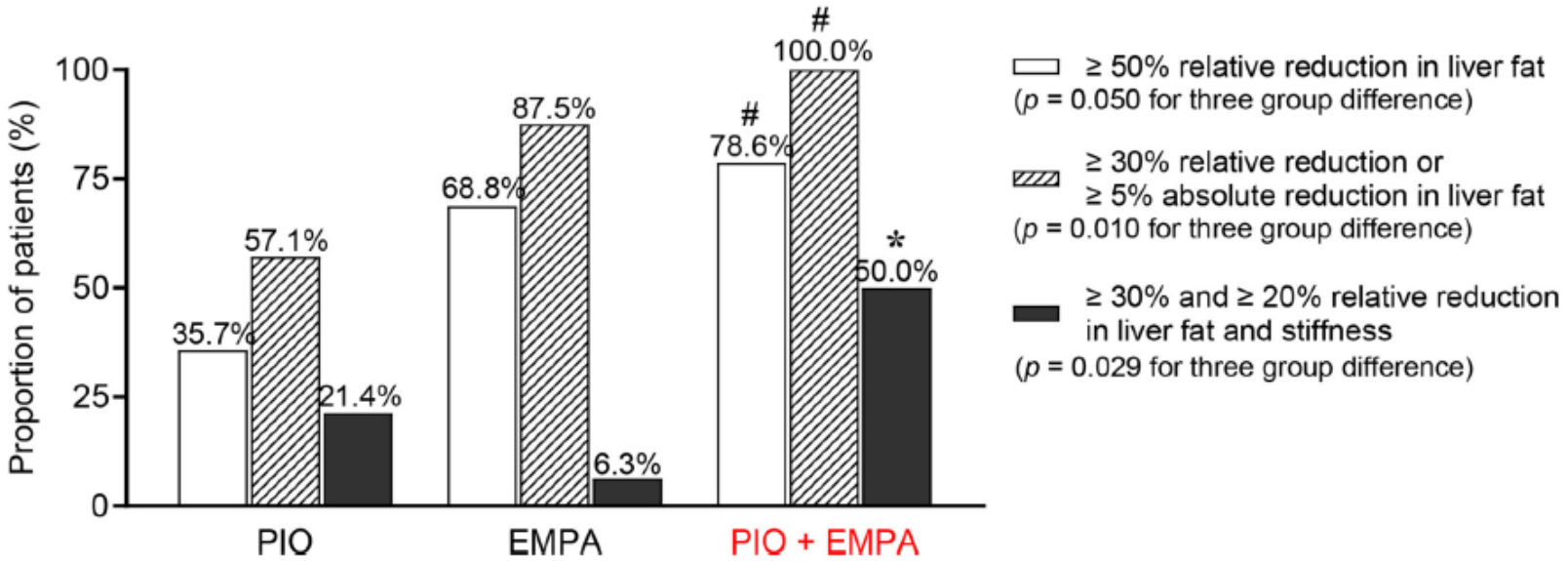
ALT



GGT



Proportion of patients with reduction in liver fat

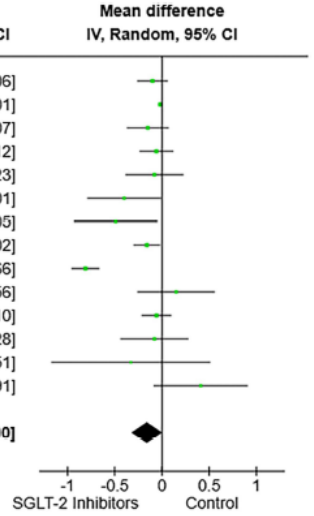


Lee M, BMC Medicine 2025

Effect of SGLT2i on Liver Fibrosis Progression in Patients with MASLD

Association between SGLT2i and FIB-4 Index in MASLD participants

Study or Subgroup	SGLT-2 Inhibitors Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
Attaran, F.2023	0.9	0.3	37	1	0.4	36	8.9%	-0.10 [-0.26 , 0.06]
Borisov, A. N.2023	1.231	0.62	4344	1.249	0.61	5787	9.9%	-0.02 [-0.04 , 0.01]
Chehrehgosha, H.2021	0.91	0.41	35	1.06	0.52	34	8.2%	-0.15 [-0.37 , 0.07]
Chehrehgosha, H.2021	0.91	0.41	35	0.97	0.37	37	8.7%	-0.06 [-0.24 , 0.12]
Hiruma, S.2023	1.12	0.49	23	1.2	0.52	19	7.0%	-0.08 [-0.39 , 0.23]
Ito, D.2017	1.21	0.48	30	1.61	1	31	5.9%	-0.40 [-0.79 , -0.01]
Ito, D.2024	1.22	0.55	32	1.71	1.19	34	5.3%	-0.49 [-0.93 , -0.05]
Khaliq, A.2024	1.04	0.43	60	1.2	0.36	60	9.1%	-0.16 [-0.30 , -0.02]
Khaliq, A.2024	1.04	0.43	60	1.85	0.4	60	9.0%	-0.81 [-0.96 , -0.66]
Shimizu, M.2019	1.32	0.88	33	1.17	0.7	24	5.7%	0.15 [-0.26 , 0.56]
Taheri, H.2020	0.775	0.293	43	0.833	0.464	47	8.9%	-0.06 [-0.22 , 0.10]
Takeshita, Y.2022	0.98	0.45	20	1.06	0.69	20	6.3%	-0.08 [-0.44 , 0.28]
Tobita, H.2021	1.04	0.31	12	1.37	1.33	10	2.4%	-0.33 [-1.17 , 0.51]
Yoneda, M.2021	1.74	0.96	21	1.33	0.63	19	4.7%	0.41 [-0.09 , 0.91]
Total (HKSJ[a])			**4785**			**6218**	**100.0%**	**-0.16 [-0.32 , 0.00]**



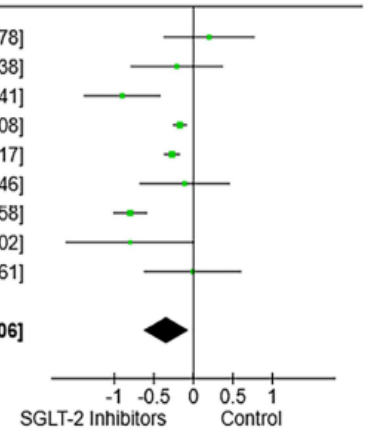
Test for overall effect: T = 2.14, df=13 (P = 0.05)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.06; Chi² = 122.07, df = 13 (P < 0.00001); I² = 90%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

16 RCT, 11,300 subjects

Association between SGLT2i and Type 4 collagen 7s in MASLD participants

Study or Subgroup	SGLT-2 Inhibitors Mean	SD	Total	Control Mean	SD	Total	Weight	Mean difference IV, Random, 95% CI
Hiruma, S.2023	4.4	1.1	23	4.2	0.8	19	8.8%	0.20 [-0.38 , 0.78]
Ito, D.2017	4	1.24	30	4.21	1.09	31	8.7%	-0.21 [-0.80 , 0.38]
Ito, D.2024	3.37	0.88	32	4.27	1.13	34	10.3%	-0.90 [-1.39 , -0.41]
Kinoshita, T.2020	4.45	0.2	32	4.62	0.17	33	17.0%	-0.17 [-0.26 , -0.08]
Kinoshita, T.2020	4.45	0.2	32	4.72	0.22	33	16.9%	-0.27 [-0.37 , -0.17]
Shimizu, M.2019	4.04	1.13	33	4.15	1.06	24	8.9%	-0.11 [-0.68 , 0.46]
Takahashi, H.2022	4.4	0.32	21	5.2	0.43	25	15.3%	-0.80 [-1.02 , -0.58]
Tobita, H.2021	3.7	0.6	12	4.5	1.2	10	5.9%	-0.80 [-1.62 , 0.02]
Yoneda, M.2021	4.01	0.88	21	4.02	1.03	17	8.2%	-0.01 [-0.63 , 0.61]
Total (HKSJ[a])			**236**			**226**	**100.0%**	**-0.35 [-0.63 , -0.06]**



Test for overall effect: T = 2.80, df=8 (P = 0.02)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² (REML[b]) = 0.09; Chi² = 39.21, df = 8 (P < 0.00001); I² = 87%

Footnotes
[a]CI calculated by Hartung-Knapp-Sidik-Jonkman method.
[b]Tau² calculated by Restricted Maximum-Likelihood method.

Yang L, Front Med 2026

Agenda

- ✓ MASLD
- ✓ Neurodegenerative diseases

Dapagliflozin and Cognitive Function in Subjects with T2D and Mild Cognitive Impairment

A prospective parallel control study

Projects	Control group (n = 40)			Dapagliflozin group (n = 40)			Difference among groups	
	Baseline	Week 36	P Value	Baseline	Week 36	P Value	P1	P2
Assessment of Cognition								
MoCA Scores (minutes)	19.65(18.00–22.00)	20.40(18.00–23.00)	0.080	20.00(18.00–22.00)	22.55(20.25–25.00)	<0.001	0.554	0.003
MMSE Scores (minutes)	23.05(21.00–25.75)	24.85(23.00–27.75)	<0.001	23.48(22.25–26.00)	26.80(26.00–29.00)	<0.001	0.338	0.003

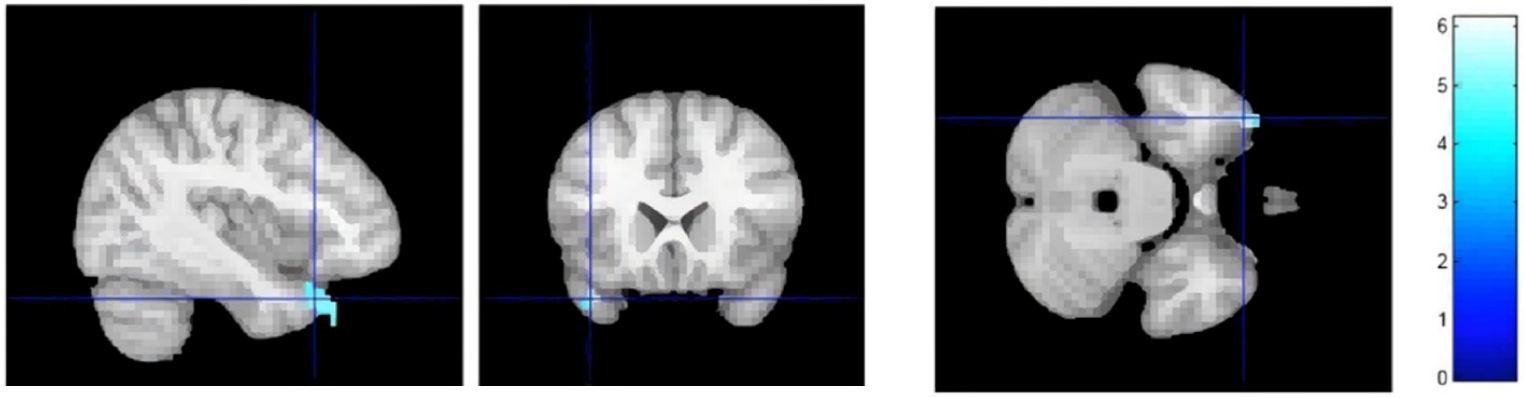


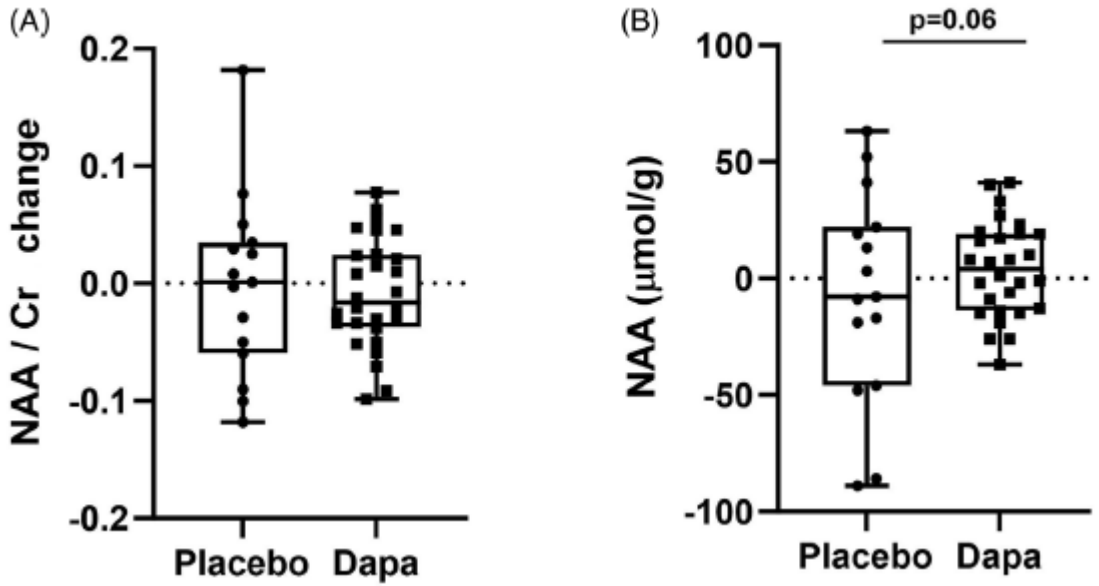
Fig. 1. ReHo difference between groups.

ReHo value in the left superior temporal gyrus was significantly lower in the dapagliflozin group than in the control group

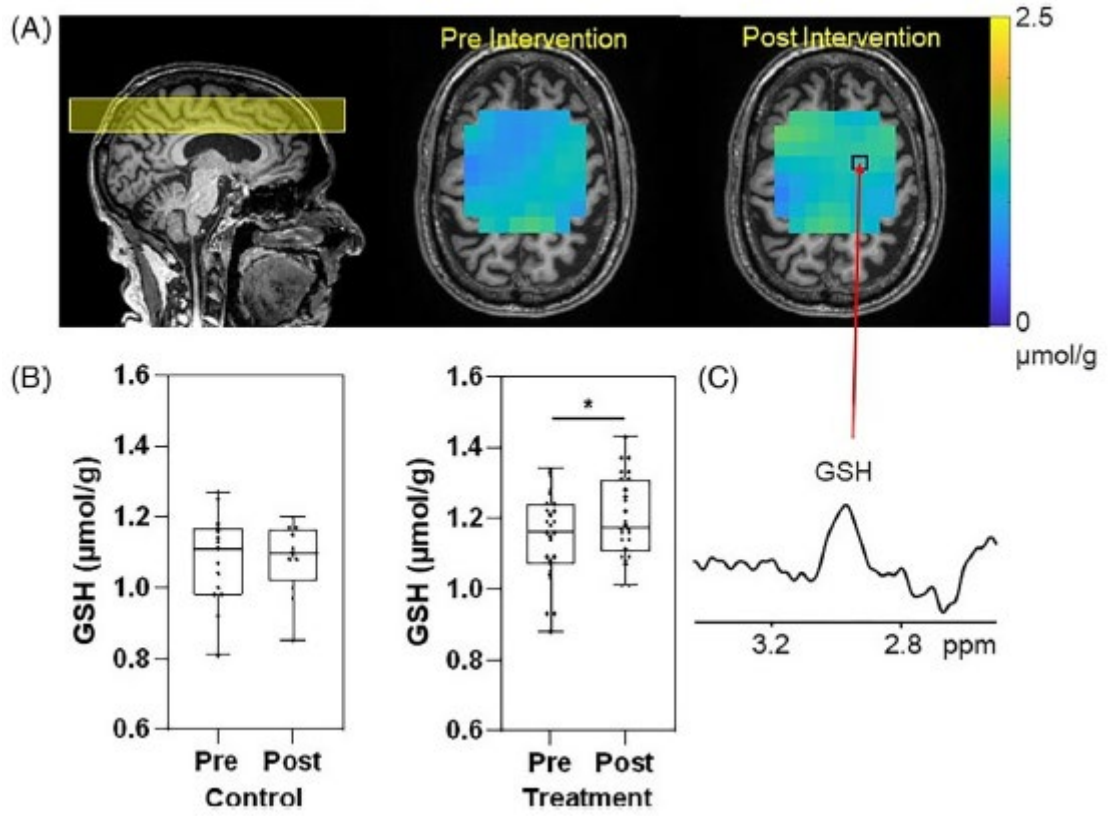
Ding J, Eur J Pharmacol 2025

Dapagliflozin in Early Alzheimer's Disease: A Randomized Controlled Trial

Magnetic resonance spectroscopy (MRS)–determined N-acetylaspartate (NAA) levels



Brain GSH measures using multiple quantum filtering (MQF) MRS technique



Burns JM, Alzheimer's Dement 2025

Potential Neuroprotective Mechanisms of SGLT2i

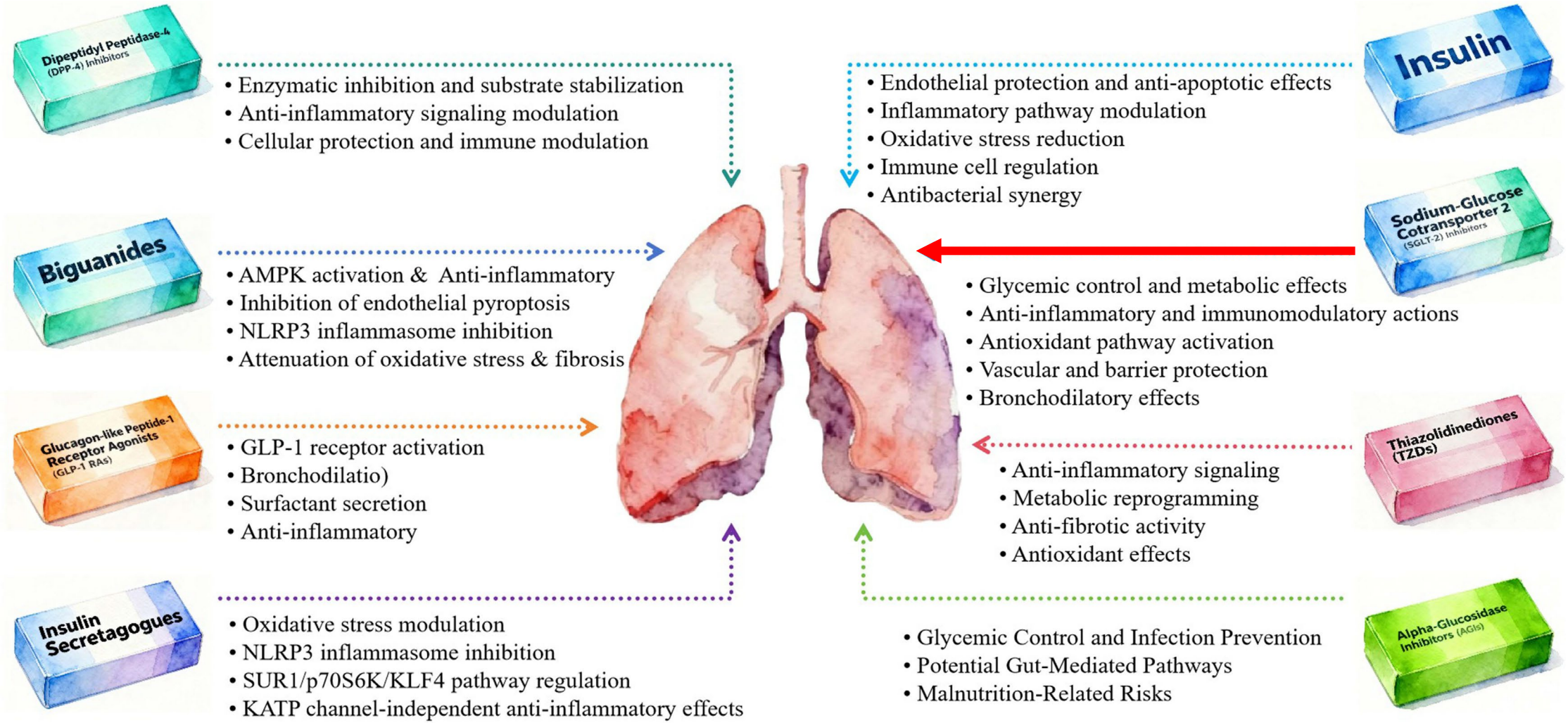
Mechanism	Description	Clinical relevance
1. Improved brain energy metabolism	Induction of mild, sustained ketosis and increased circulating β-hydroxybutyrate (BHB) levels via enhanced fatty acid oxidation and reduced insulin levels	Enhances mitochondrial adenosine triphosphate (ATP) production, reduces oxidative stress, and supports neuronal function under insulin-resistant conditions
2. Reduction of neuroinflammation	Inhibits microglial and astrocyte activation, decreases pro-inflammatory cytokines (e.g., IL-6, TNF-α, IL-1β), and downregulates NF-κB signaling pathways	Prevents or slows neuronal damage, protects synaptic integrity, and mitigates progression of neurodegenerative pathology
3. Amelioration of insulin resistance and oxidative stress	Improves systemic and possibly central insulin sensitivity; reduces mitochondrial reactive oxygen species (ROS); upregulates antioxidant defenses (e.g., SOD, catalase)	Supports synaptic plasticity, inhibits tau hyperphosphorylation, and reduces oxidative injury to neurons
4. Enhancement of cerebral perfusion and vascular health	Lowers blood pressure, reduces arterial stiffness, and improves endothelial function	Promotes cerebral blood flow and may reduce risk of vascular cognitive impairment, especially in mixed dementia
5. Potential modulation of amyloid and tau pathways	May reduce amyloid-β accumulation and tau phosphorylation via enhanced autophagy, improved insulin signaling, and reduced oxidative stress in animal models	Targets core pathological processes in Alzheimer's disease; potential for disease modification
6. Preservation of blood–brain barrier (BBB) integrity	Decreases systemic inflammation and oxidative stress; improves endothelial stability	Helps prevent neuroinflammation and restricts entry of neurotoxins into the CNS, especially relevant in metabolic and vascular comorbidities

Kostrzewska P, Neurol Ther 2025

Agenda

- ✓ MASLD
- ✓ Neurodegenerative diseases
- ✓ Respiratory disease outcomes

Core Mechanisms of Major Hypoglycemic Agents in Regulating Pulmonary Pathophysiology



Yang Y, J Inflamm Res 2025

Dapagliflozin, HF with Mildly Reduced/Preserved Ejection Fraction, and COPD

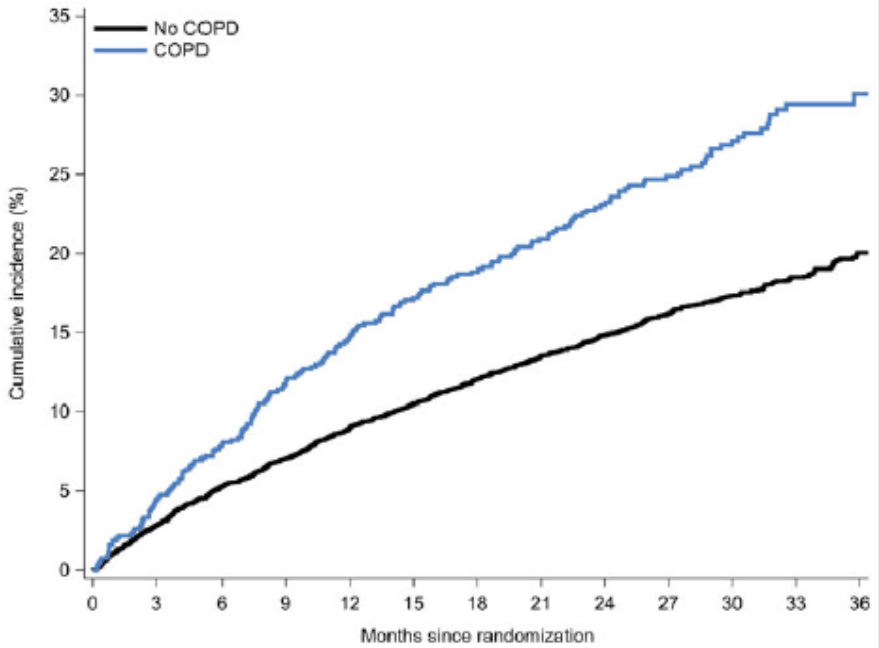
6,261 patients in DELIVER

694 (11.1%) patients had an investigator-reported history of mild-to-moderate chronic obstructive pulmonary disease

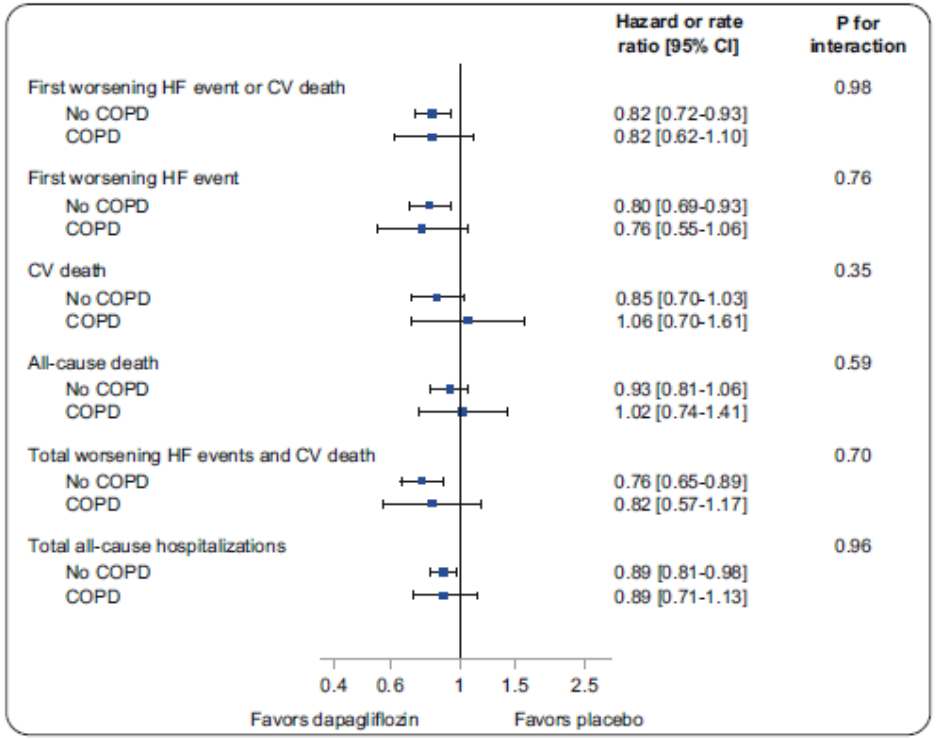
Characteristics of patients with versus without COPD

- ↑ Age
- ↑ Men
- ↑ Smokers
- ↑ BMI
- ↑ Atrial fibrillation
- ↑ Atherosclerotic disease
- ↑ Valvular heart disease
- ↑ Hypertension
- ↑ Prior HF hospitalization
- ↑ Duration of HF
- ↓ Health-related quality of life
- \- Similar LVEF
- \- Similar NT-proBNP level

Association between COPD and first worsening HF event or CV death



Effects of dapagliflozin compared with placebo on outcomes according to COPD status

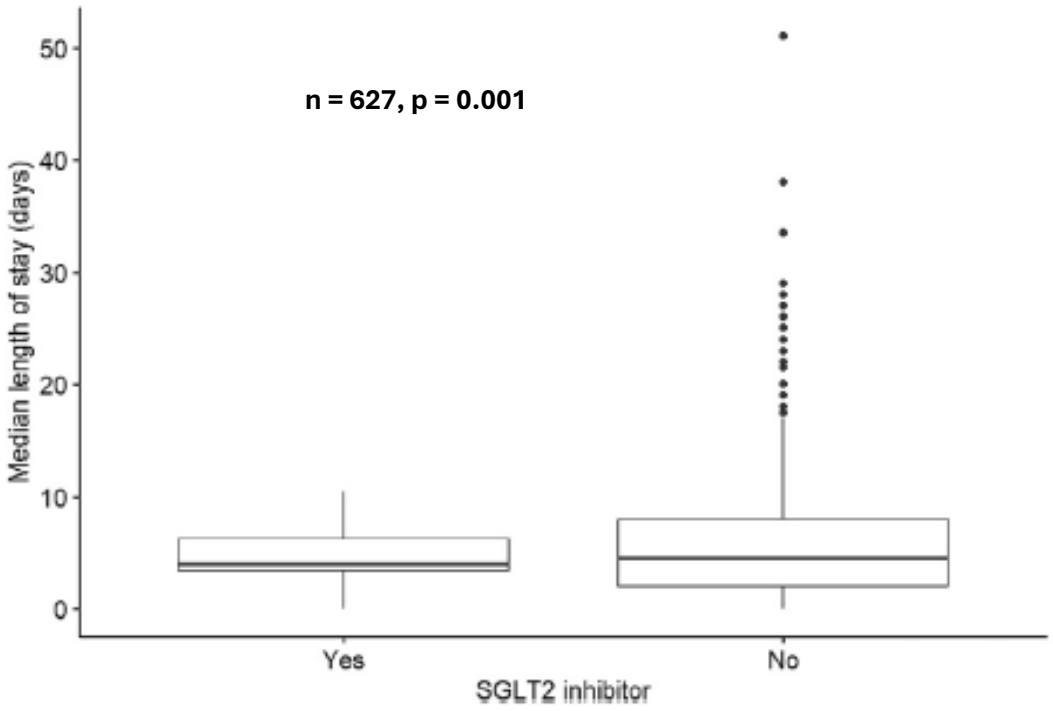


Butt JH, Eur Journ Heart Fail 2023

SGLT2i and Admission, Frequency, Duration and Use of Acute Non-Invasive Ventilation in Patients with COPD

A single-centre 24-month retrospective observational study in a UK tertiary care centre

Median length of stay by SGLT2i prescription



Multivariate model output of median length of stay

Associations	Median length of stay (days)		
	Incidence rate ratios	CI	*p*
SGLT2-inhibitor prescription	0.74	0.62–0.88	0.001
Age (years)	1.02	1.02–1.02	<0.001
Sex (male vs female)	1.06	0.99–1.13	0.104
$FEV_{1\%}$ predicted	0.99	0.99–0.99	<0.001
Congestive cardiac failure	1.12	1.04–1.21	0.002
Type 2 diabetes mellitus	0.92	0.85–1.01	0.068
Long-term macrolide use	1.14	1.02–1.26	0.016
Observations	625		
R^2 Nagelkerke	0.274		

SGLT2i, sodium/glucose co-transporter-2 inhibitors; CCF, congestive cardiac failure; T2DM, type 2 diabetes mellitus.

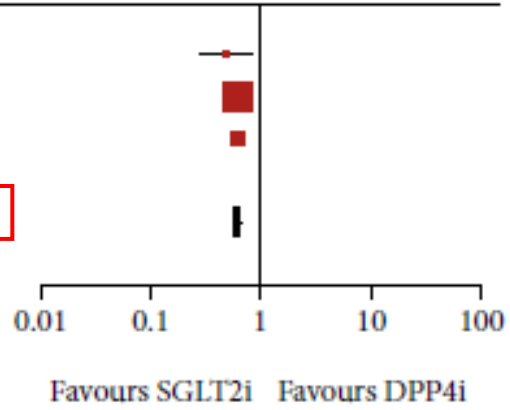
Kan A, Clinical Medicine 2026

SGLT2i and the Risk of Pneumonia in T2D

Association between SGLT2i use with pneumonia

Study or subgroup	Log (HR)	SE	SGLT2i Total	DPP4i Total	Weight	Hazard ratio IV, fixed, 95% CI
Brunetti 2021	−0.733969	0.274116	1011	5552	1.7%	0.48 [0.28, 0.82]
Jeong 2023	−0.494296	0.041915	205534	205534	71.7%	0.61 [0.56, 0.66]
Wu 2022	−0.462035	0.068709	10706	18281	26.7%	0.63 [0.55, 0.72]
Total (95% CI)			217251	229367	100.0%	0.61 [0.57, 0.66]

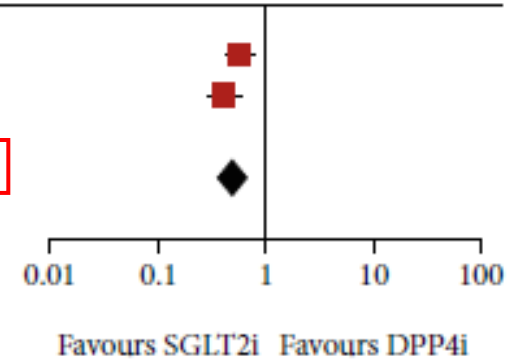
Heterogeneity: $\chi^2 = 0.97$, df = 2 (P = 0.62); $I^2 = 0\%$
Test for overall effect: Z = 13.80 (P < 0.00001)
Test for subgroup differences: not applicable



Association between SGLT2i use with pneumonia mortality

Study or subgroup	Log (HR)	SE	SGLT2i Total	DPP4i Total	Weight	Hazard ratio IV, random, 95% CI
Au 2022	−0.562119	0.154629	6664	26656	53.4%	0.57 [0.42, 0.77]
Wu 2022	−0.891598	0.176827	10706	18281	46.6%	0.41 [0.29, 0.58]
Total (95% CI)			17370	44937	100.0%	0.49 [0.35, 0.67]

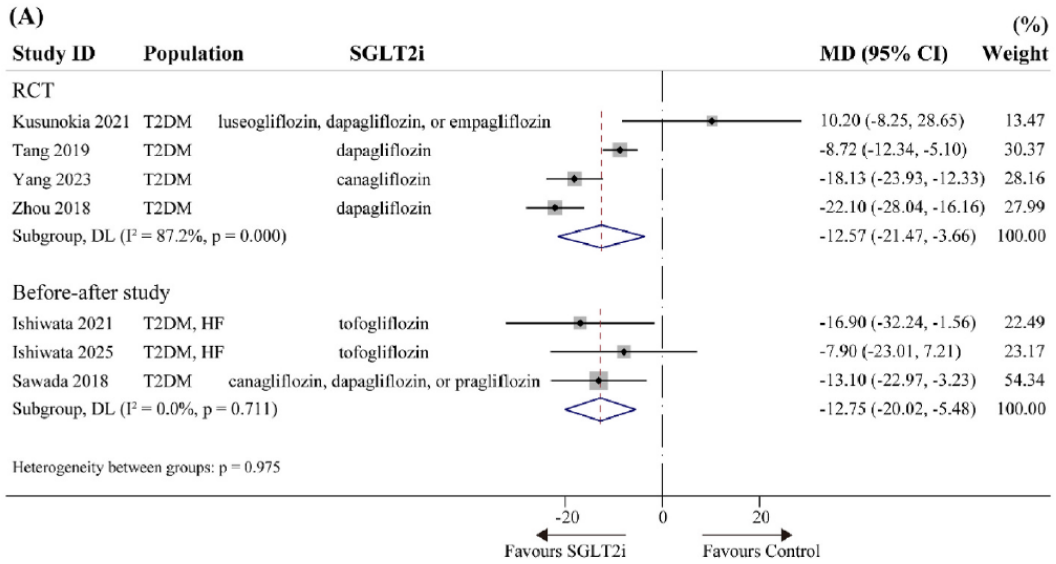
Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 1.97$, df = 1 (P = 0.16); $I^2 = 49\%$
Test for overall effect: Z = 4.35 (P < 0.0001)
Test for subgroup differences: not applicable



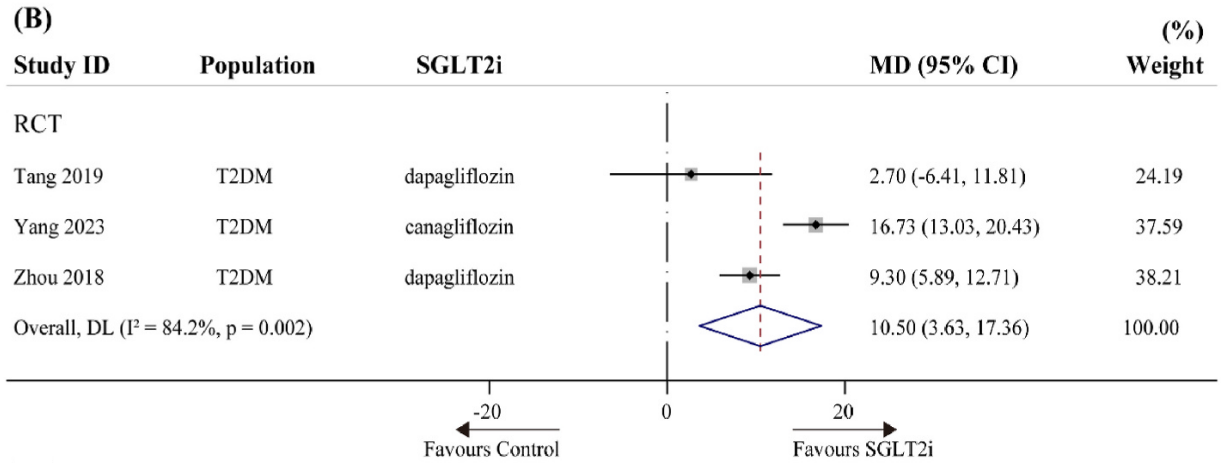
Alfonso Arvez MJ, J Diabetes Res 2025

SGLT2i for Obstructive Sleep Apnea in Patients with T2D

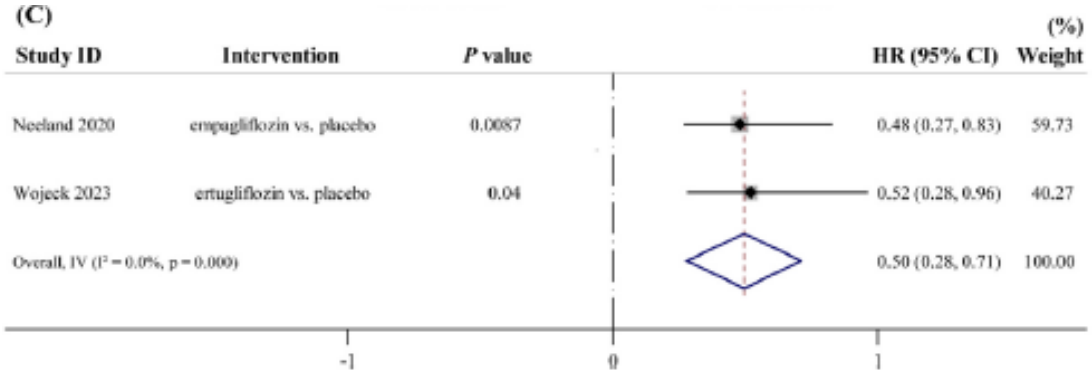
Apnea-Hypopnea Index (AHI) outcome



Lowest SpO2 outcome



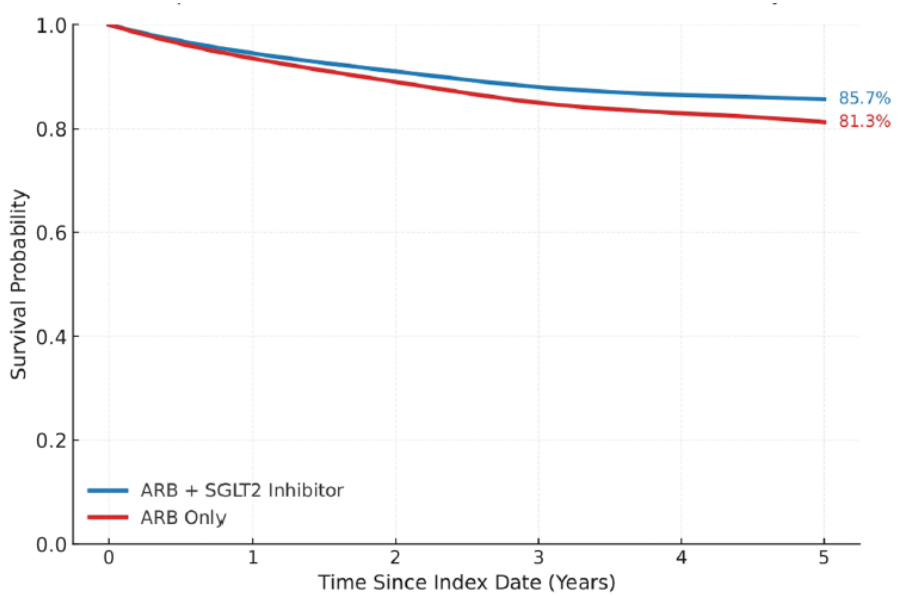
Time to first OSA event



Yang R, Sleep Medicine 2026

Repurposing SGLT2i in Sarcoidosis: A Potential Strategy for Reducing Mortality

5-Year All-Cause Mortality



Risk analysis of clinical outcomes

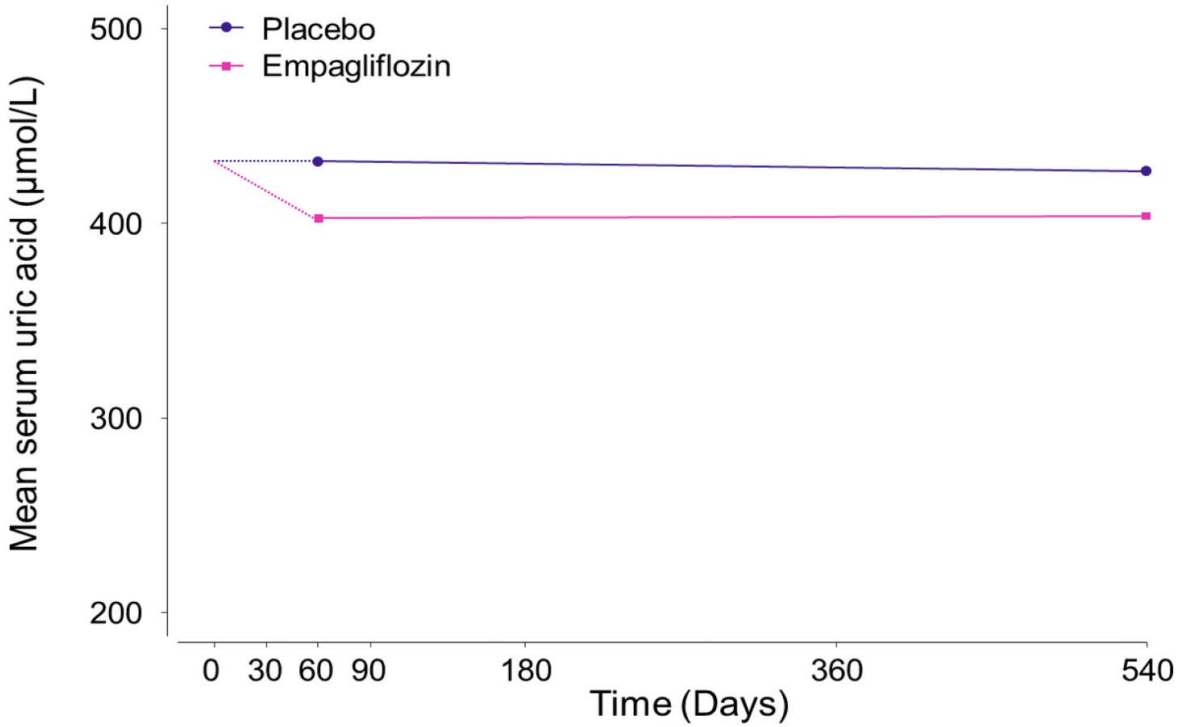
Outcome	Survival Probability at the end of time window		Log-Rank Test (df = 1)		Hazard Ratio (HR) and Proportionality (df = 1)			
	Patients with ARBs + SGLT2- Inhibitors (n = 4733)	Patients with ARBs (n = 4733)	χ^2	p	HR	95 % CI	χ^2	p
All-cause mortality (5-year)	85.70 %	81.28 %	5.764	0.016	0.839	(0.727, 0.968)	1.459	0.227
Respiratory failure	80.21 %	80.22 %	0.001	0.974	1.003	(0.862, 1.166)	0.020	0.889
Cardiac arrest	95.43 %	95.89 %	0.029	0.865	0.975	(0.725, 1.311)	0.864	0.353
Acute MI	88.74 %	89.82 %	0	0.994	1.001	(0.818, 1.224)	1.324	0.250
Acute heart failure	80.75 %	82.82 %	0.099	0.753	1.027	(0.869, 1.214)	3.316	0.069
Cerebral infarction	89.81 %	91.24 %	0.575	0.448	1.089	(0.873, 1.359)	1.007	0.316
Acute kidney injury	73.17 %	74.30 %	0.645	0.422	1.057	(0.923, 1.211)	0.005	0.945
Sepsis	83.10 %	83.87 %	0	0.994	0.999	(0.851, 1.174)	0.105	0.746

Nasibul Alam ABM, Heart Lung 2026

Agenda

- ✓ MASLD
- ✓ Neurodegenerative diseases
- ✓ Respiratory disease outcomes
- ✓ Relevant clinical implications of the anti-inflammatory effect

Empagliflozin Lowers Serum Uric Acid in CKD: Exploratory Analyses from the EMPA-KIDNEY Trial



P for interaction with time = 0.007

Maximum effect in subjects without T2D and relatively preserved kidney function

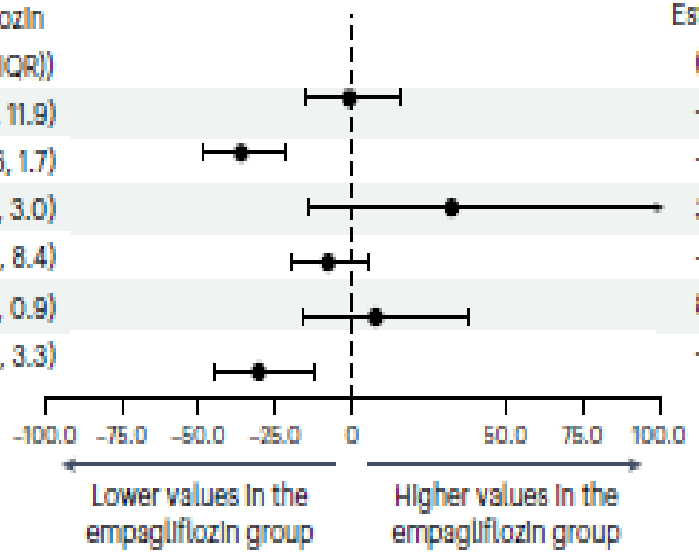
	Empagliflozin Mean (SE), µmol/L*	Placebo Mean (SE), µmol/L*	Absolute Difference (95% CI), µmol/L*	P
2 months	402.9 (1.7)	431.9 (1.6)	-29.0 (-33.5, -24.4)	
18 months	403.6 (2.2)	427.0 (2.2)	-23.4 (-29.5, -17.3)	
Overall	**403.3 (1.7)**	**428.9 (1.6)**	**-25.6 (-30.3, -21.0)**	**<0.001**

Mayne KJ, Nephrol Dial Transplant 2025

Empagliflozin in Nondiabetic Individuals with Calcium and Uric Acid Kidney Stones: a Randomized Phase 2 Trial

Primary analysis in participants with calcium and UA kidney stones

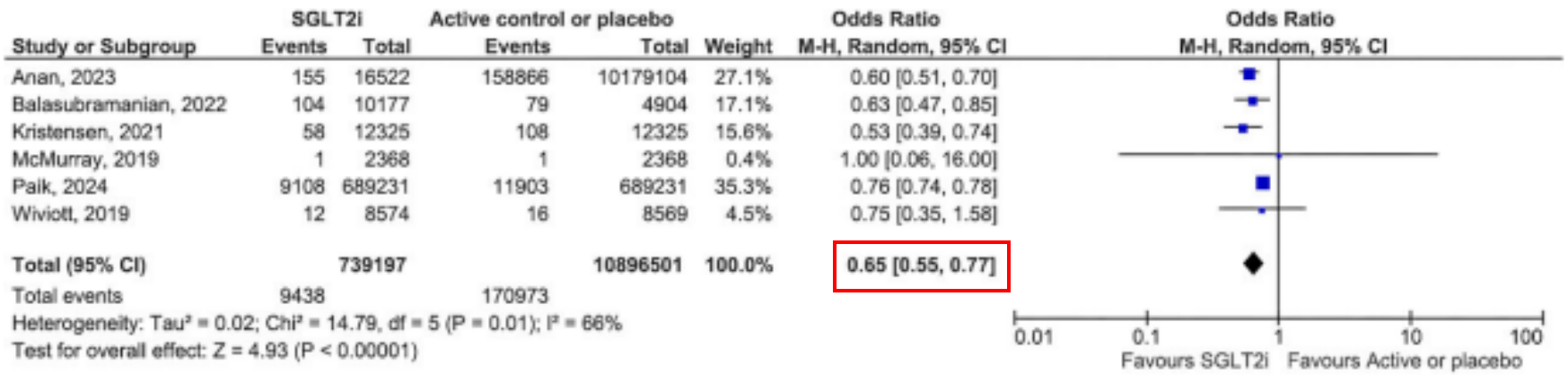
Type of SF	Primary outcomes	N[a]	Placebo (median (IQR))	N[b]	Empagliflozin (median (IQR))	Estimated relative difference (% (95% CI))[c]	P value[d]
Calcium	Calcium oxalate supersaturation	25	8.9 (7.7, 13.4)	25	9.1 (7.3, 11.9)	−1 (−15 to 16)	0.921
Calcium	Calcium phosphate supersaturation	25	1.9 (1.0, 2.7)	25	1.0 (0.6, 1.7)	−36 (−48 to −21)	<0.001*
Calcium	UA supersaturation	25	1.3 (0.9, 2.3)	25	2.2 (1.1, 3.0)	32 (−14 to 104)	0.204
UA	Calcium oxalate supersaturation	21	6.6 (4.4, 10.0)	21	5.8 (4.4, 8.4)	−8 (−19 to 5)	0.236
UA	Calcium phosphate supersaturation	21	0.5 (0.3, 0.8)	21	0.4 (0.3, 0.9)	8 (−16 to 38)	0.559
UA	UA supersaturation	21	3.3 (2.6, 5.4)	21	2.5 (1.8, 3.3)	−30 (−44 to −12)	0.002



Anderegg MA, Nature Med 2025

SGLT2 Inhibitors and Nephrolithiasis Risk: a Meta-Analysis

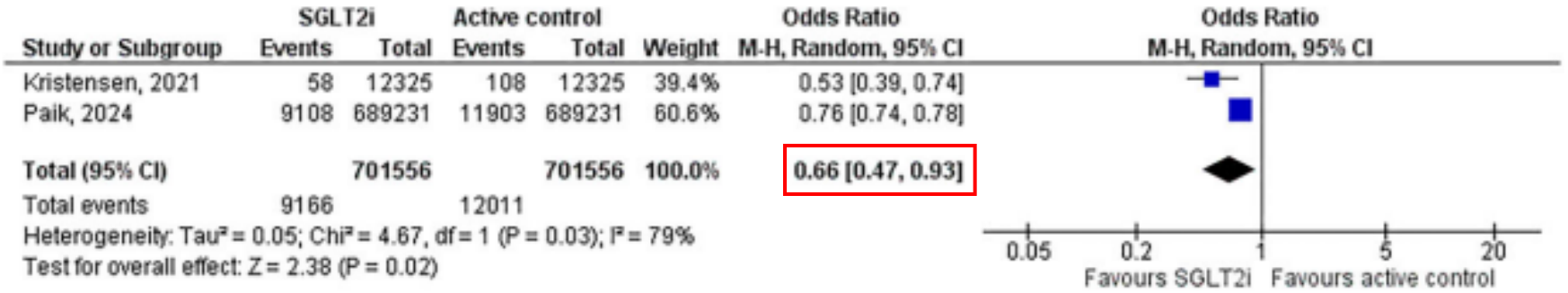
Risk of nephrolitiasis in the SGLT2i group compared with the control group (active control, placebo or no therapy)



Study or Subgroup	SGLT2i Events	SGLT2i Total	Active control or placebo Events	Active control or placebo Total	Weight	Odds Ratio M-H, Random, 95% CI
Anan, 2023	155	16522	158866	10179104	27.1%	0.60 [0.51, 0.70]
Balasubramanian, 2022	104	10177	79	4904	17.1%	0.63 [0.47, 0.85]
Kristensen, 2021	58	12325	108	12325	15.6%	0.53 [0.39, 0.74]
McMurray, 2019	1	2368	1	2368	0.4%	1.00 [0.06, 16.00]
Paik, 2024	9108	689231	11903	689231	35.3%	0.76 [0.74, 0.78]
Wiviott, 2019	12	8574	16	8569	4.5%	0.75 [0.35, 1.58]
Total (95% CI)		**739197**		**10896501**	**100.0%**	**0.65 [0.55, 0.77]**
Total events	9438		170973			

Heterogeneity: Tau² = 0.02; Chi² = 14.79, df = 5 (P = 0.01); I² = 66%
Test for overall effect: Z = 4.93 (P < 0.00001)

Risk of nephrolitiasis in the SGLT2i group compared with the active control group (GLP-1RA and DPPi)

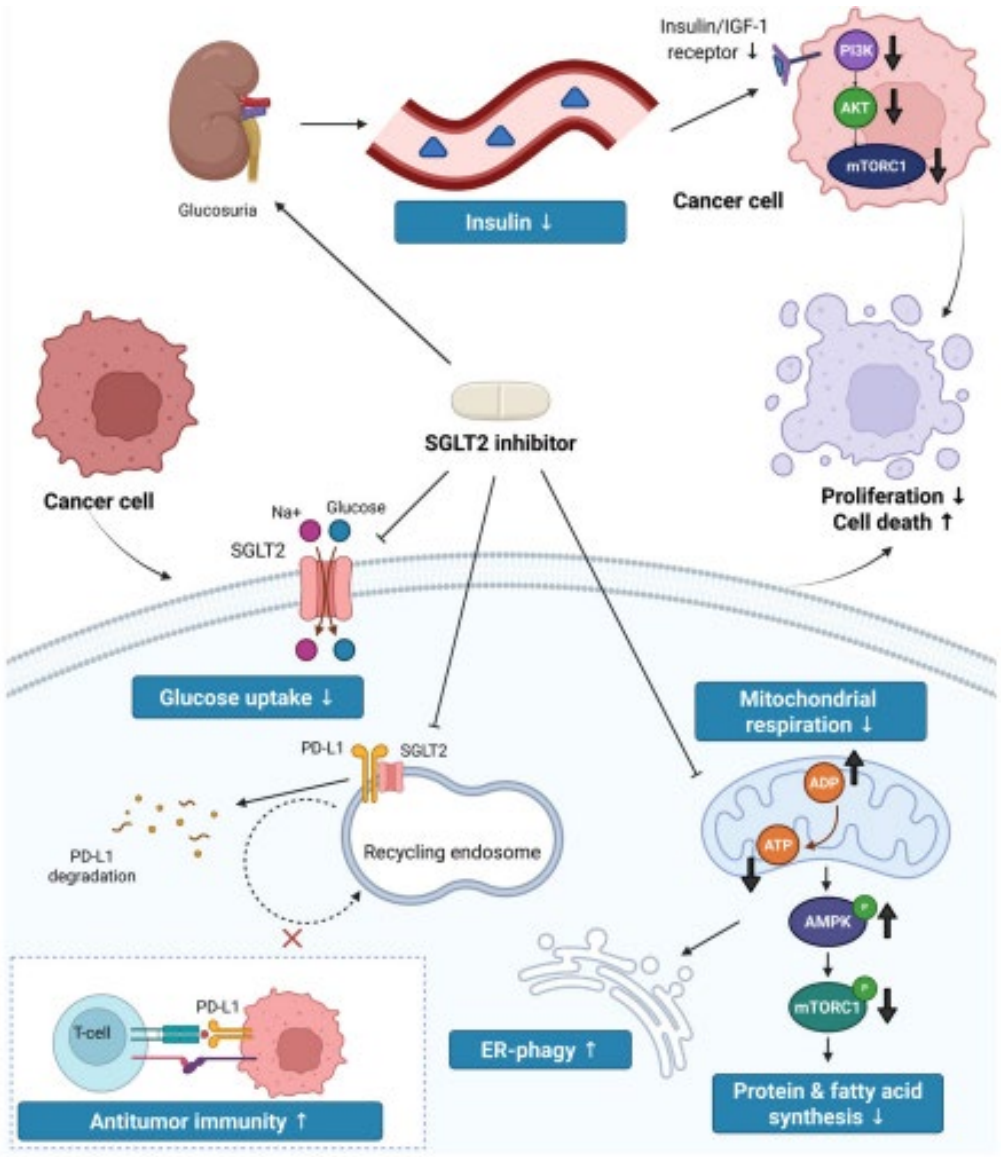


Study or Subgroup	SGLT2i Events	SGLT2i Total	Active control Events	Active control Total	Weight	Odds Ratio M-H, Random, 95% CI
Kristensen, 2021	58	12325	108	12325	39.4%	0.53 [0.39, 0.74]
Paik, 2024	9108	689231	11903	689231	60.6%	0.76 [0.74, 0.78]
Total (95% CI)		**701556**		**701556**	**100.0%**	**0.66 [0.47, 0.93]**
Total events	9166		12011			

Heterogeneity: Tau² = 0.05; Chi² = 4.67, df = 1 (P = 0.03); I² = 79%
Test for overall effect: Z = 2.38 (P = 0.02)

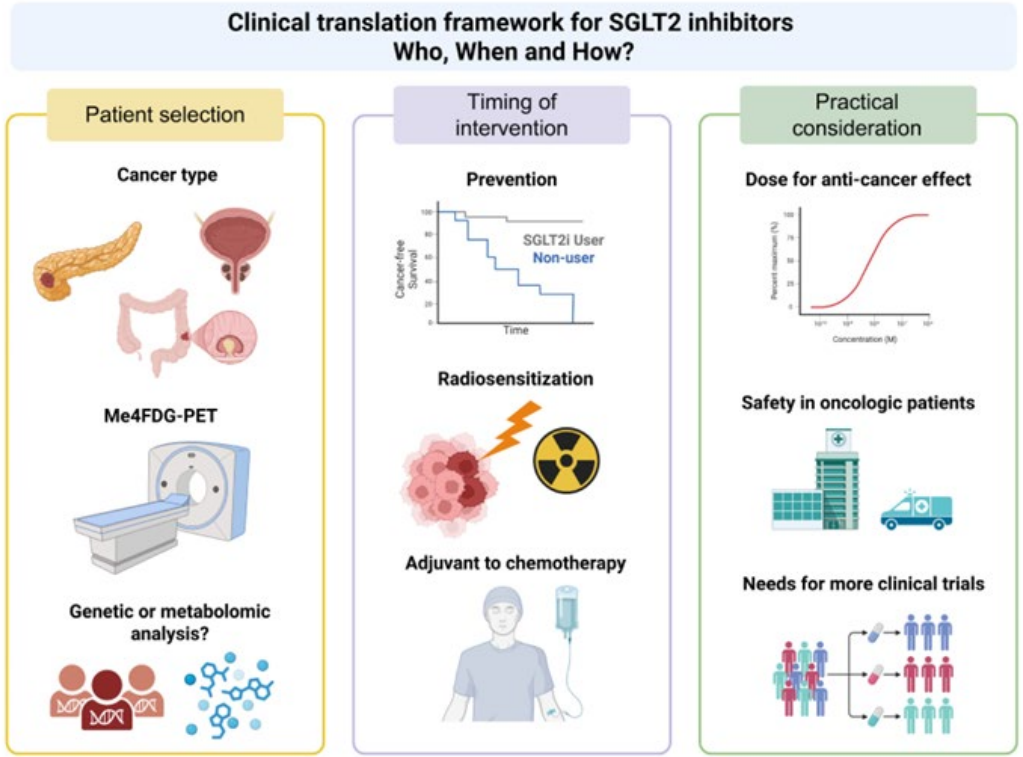
Kanbay M, Nephrol Dial Transplant 2025

SGLT2i as Emerging Anticancer Agents



Highlights

- SGLT2 inhibitors emerge as promising anticancer drug candidates.
- SGLT2 inhibition decreases tumor glucose uptake and disrupts mitochondrial function in cancer cells.
- These agents also enhance antitumor immunity by promoting PD-L1 degradation.
- Observational studies suggest reduced risks of pancreatic and prostate cancers.
- Future strategies for biomarker-guided patient selection and monitoring are needed.



Cho YK, Diabetes Metab J 2026

Clinical Evidence of SGLT2i and Cancer Outcomes

Study design	Population	Comparator	Cancer outcome assessed	Main findings
RCTs and meta-analyses	>100,000 patients with T2DM from large-scale CV/renal outcome trials	Placebo/active comparators	Overall cancer incidence, cancer mortality	Neutral effect; no increased risk of overall or site-specific cancers
Observational cohort (Korea, pancreatic cancer)	Korean NHIS, nationwide (new SGLT2i users)	Other GLDs	Pancreatic cancer incidence	Reduced pancreatic cancer risk in new SGLT2i users
Observational cohort (Korea, prostate cancer)	Korean NHIS, nationwide (new SGLT2i users)	Other GLDs	Prostate cancer incidence	Reduced prostate cancer risk in SGLT2i users, particularly in non-obese individuals
Observational cohort (Hong Kong)	42,129 male patients with T2DM	DPP-4 inhibitors	Prostate cancer incidence, cancer mortality	55% lower risk of prostate cancer; reduced cancer-related and all-cause mortality
Observational cohort (Japan)	Nationwide claims data, PSM matched	DPP-4 inhibitors	Overall cancer, CRC incidence	No increased risk overall; signals of reduced CRC with SGLT2i
Observational (multinational, TriNetX)	MASLD+T2DM (n=187,860)	Active comparators (various GLDs)	HCC incidence, mortality	57% reduced risk of HCC; lower risk of fibrosis and all-cause mortality
Observational (Hong Kong)	T2DM+SGLT2i vs. DPP-4 inhibitor (n=62,699)	DPP-4 inhibitors	HCC incidence	58% lower risk of HCC; benefit consistent in HBV/HCV and cirrhosis subgroups
Observational (Korea)	T2DM+fatty liver (n=201,542)	Non-SGLT2i users	HCC incidence	Neutral in general NAFLD; Significant reduction in the high-risk group (fatty liver+viral hepatitis)
Observational (UK CPRD)	T2DM new users (n=221,170)	DPP-4 inhibitors	Lung cancer incidence	Neutral effect (HR, 0.96) over a median of 2.4 years follow-up
Systematic review of observational studies	Multiple population cohorts and registries	Various GLDs (esp. DPP-4 inhibitors)	Site-specific cancer risks	Neutral to favorable association; lower risks for liver, lung, and prostate cancers
Mendelian randomization	Genetic proxies for SGLT2 inhibition; circulating metabolites	-	Prostate cancer risk	Genetically proxied inhibition linked to reduced prostate cancer risk
Translational pilot study	Advanced pancreatic adenocarcinoma patients	Chemotherapy± dapagliflozin	Safety, feasibility, metabolic outcomes	Well tolerated; no unexpected toxicity; favorable metabolic modulation
Real-world translational study	GI cancer patients receiving chemo- or radiotherapy	±SGLT2i (concurrent use)	Survival, treatment tolerance	Improved overall survival, fewer hospitalizations, reduced complications

Cho YK, Diabetes Metab J 2026

Conclusion

SGLT2i appear to function as systemic metabolic modulators with expanding therapeutic potential:

- ✓ Liver: likely mediated by weight reduction, improved insulin sensitivity, and favorable shifts in hepatic energy metabolism
- ✓ Lung: osmotic diuresis, reduced interstitial edema, and systemic anti-inflammatory effects
- ✓ Brain: improvements in cerebral vascular function, metabolic regulation, and attenuation of systemic inflammation and oxidative stress