



XXXII Corso Nazionale di Aggiornamento Dialisi e Tecnologia

“Nuove Opportunità per Vecchi Avversari”

Nuove strategie farmacologiche
dell'obesità in dialisi: quale spazio?

F. Laurendi
Dirigente Medico I livello,
SOC Nefrologia ASL VCO



Nephron

11,7%

23
3
2, 2023



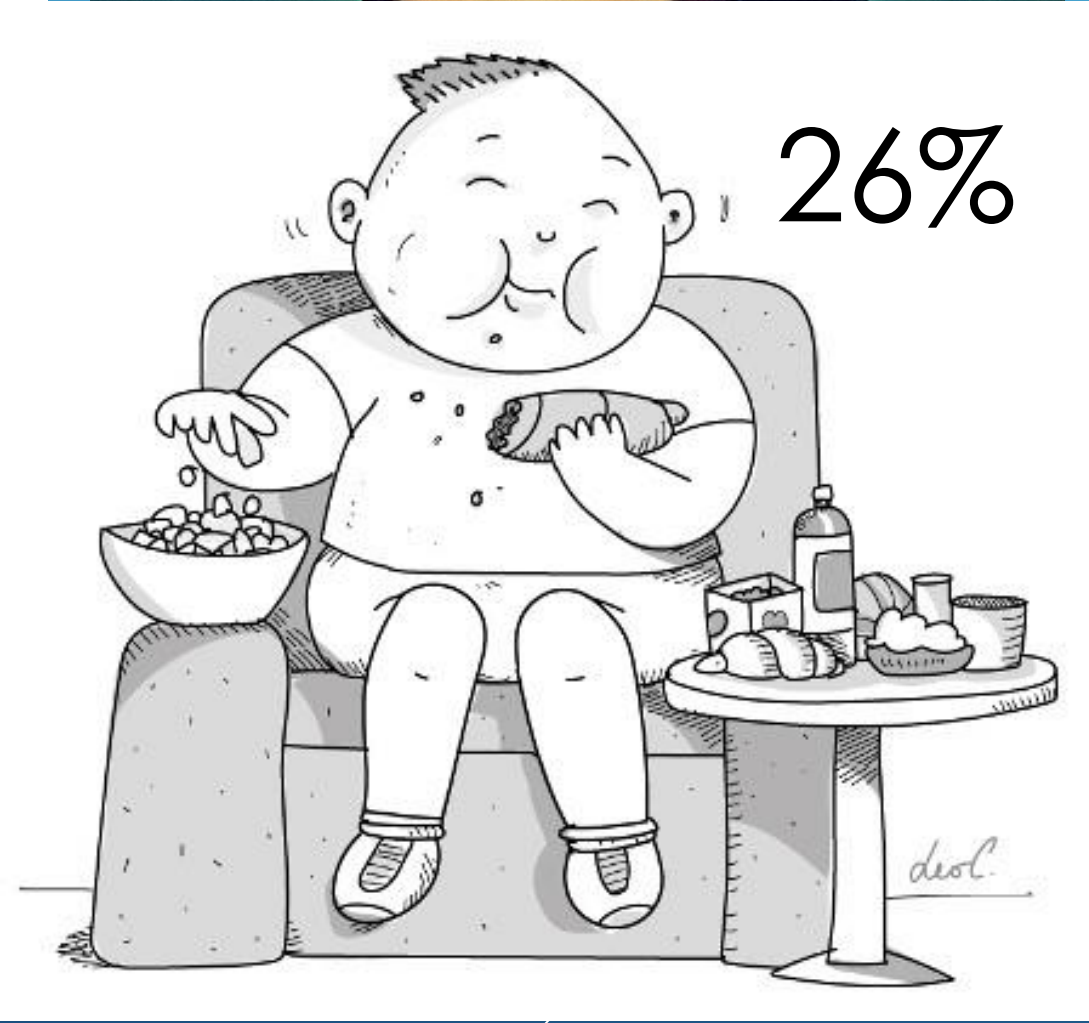
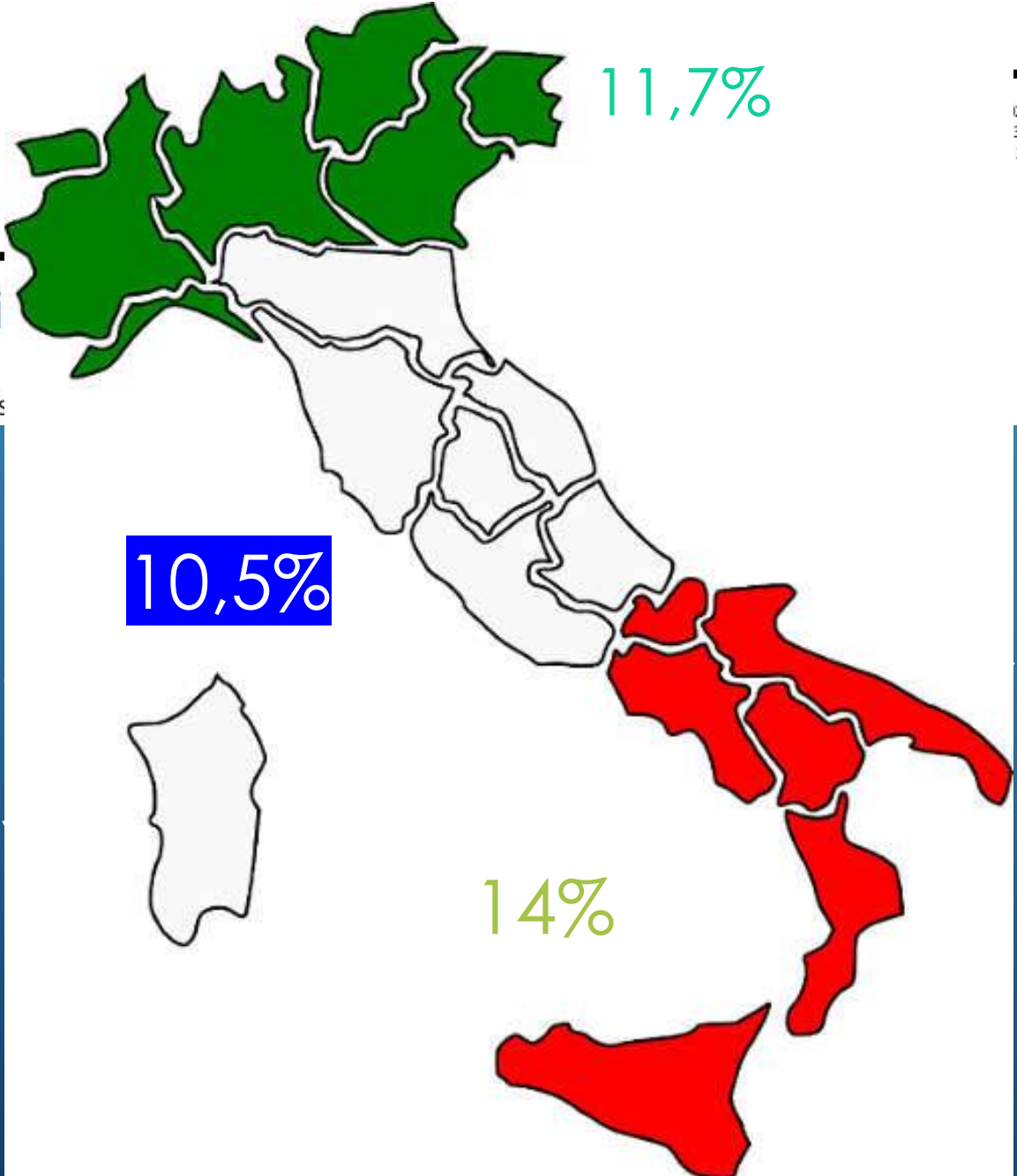
Chroni

Radovan Hojs

10,5%

- Ob
- Pre

14%



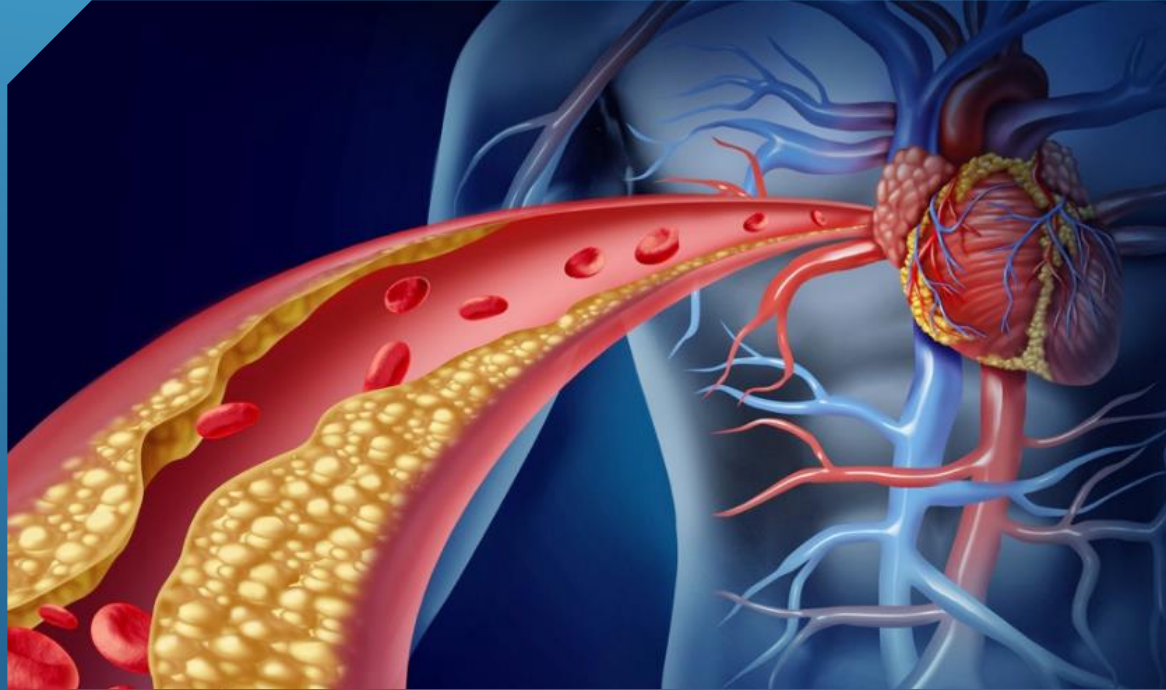
Body Mass Index and Risk for End-Stage Renal Disease

Chi-yuan Hsu, MD, MSc; Charles E. McCulloch, PhD; Carlos Iribarren, MD, MPH, PhD; Jeanne Darbinian, MPH; and Alan S. Go, MD

Fattore di rischio progressione CKD fino a ESRD:

- BMI normale (18.5-24.9): rischio base
- Sovrappeso (25.0-29.9): 1.87 volte maggiore
- Obesità classe I (30.0-34.9): 3.57 volte maggiore
- Obesità classe II (35.0-39.9): 6.12 volte maggiore
- Obesità Classe III (≥ 40): 7.07 volte maggiore





«OBESITY PARADOX»: MIGLIORE SOPRAVVIVENZA IN DIALISI, MA CORRELATA A MALATTIE CARDIACHE E DISMETABOLICHE

DOI: 10.1111/sdi.12834

EDITORIAL

Seminars in Dialysis

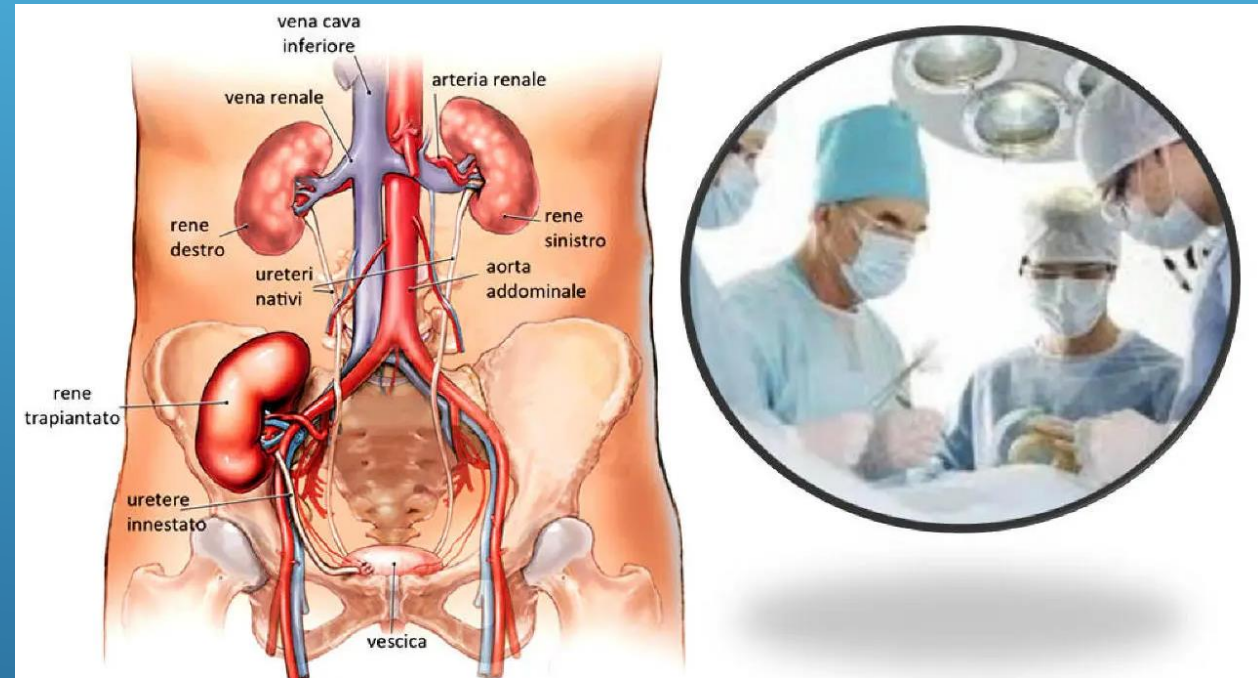
WILEY

The obesity paradox: A further consideration in dialysis patients

Obesity Impacts Access to Kidney Transplantation

Dorry L. Segev,* Christopher E. Simpkins,* Richard E. Thompson,[†] Jayme E. Locke,* Daniel S. Warren,* and Robert A. Montgomery*

- Maggiore attesa in LAT (fino a 59 mesi)
- Maggiore sviluppo di comorbidità (IA, DM)
- Ritardo di guarigione sito chirurgico
- Delayed Graft Function
- Early failure



American Journal of Transplantation 2015; 15: 1360–1368
Wiley Periodicals Inc.

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and the American Society of Transplant Surgeons

doi: 10.1111/ajt.13116

Addressing Morbid Obesity as a Barrier to Renal Transplantation With Laparoscopic Sleeve Gastrectomy

• Cut-off BMI <30

• Programma dietetico

• Approccio chirurgico

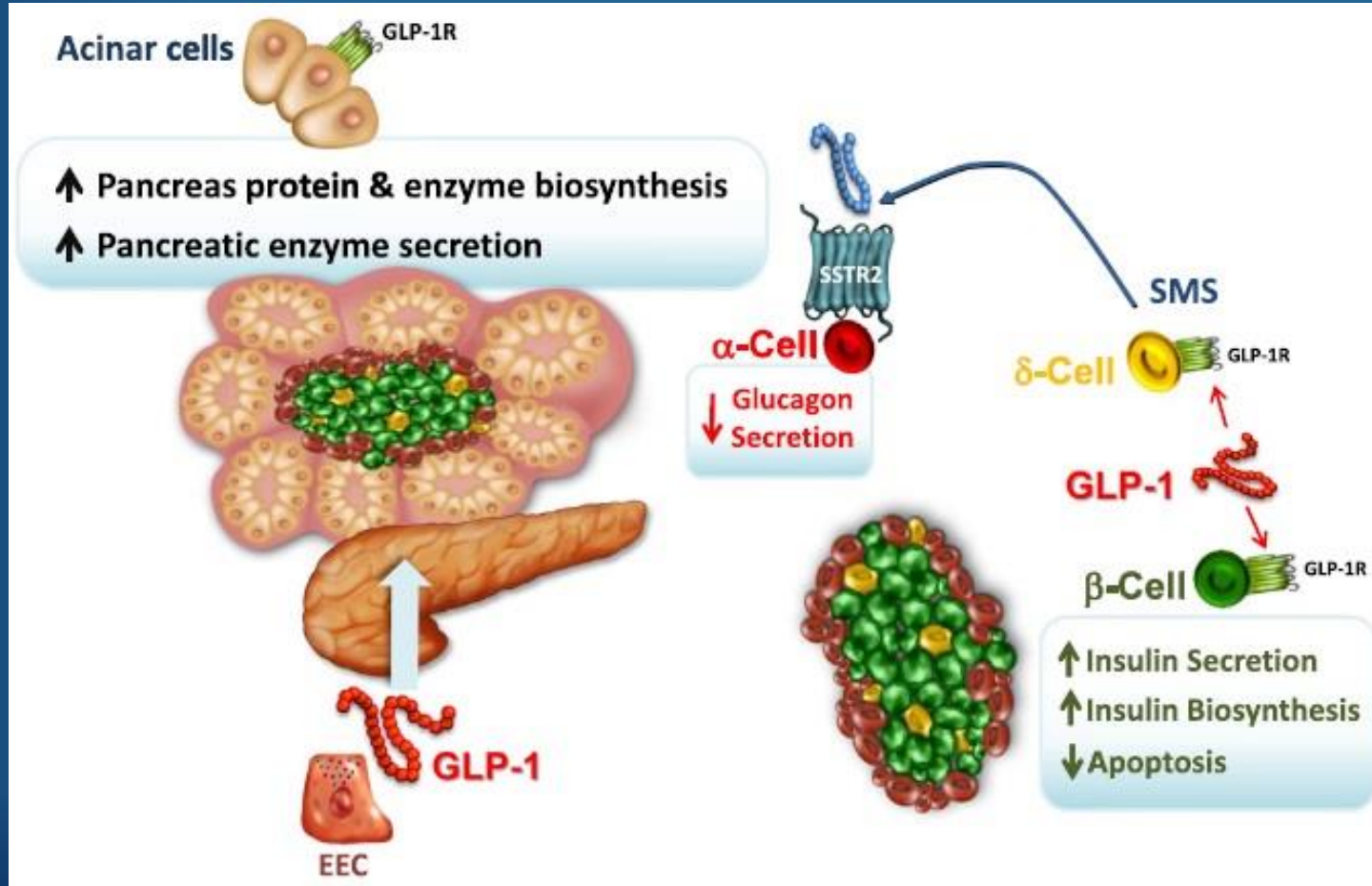
The background features a blurred image of several white and orange capsules scattered on a light-colored surface. Overlaid on this is a dark blue grid of hexagons, with one hexagon in the upper left being a lighter shade. On the right side, there are several thin, white, parallel diagonal lines.

TERAPIA FARMACOLOGICA

GLP-1

Mechanisms of Action and Therapeutic Application of Glucagon-like Peptide-1

Daniel J. Drucker^{1,*}



GLP-1

- Aumenta il rilascio di insulina

- Inibisce la secrezione di glucagone

- Stimola la proliferazione delle cellule β

- Inibisce l'apoptosi delle cellule β

- Aumenta il rilascio di somatostatina

- Interagisce con i centri regolatori della fame

- Aumenta il senso di sazietà

- Riduce l'appetito

- Inibisce la gluconeogenesi epatica

- Riduce la steatosi e la fibrosi epatica

- Rallenta la velocità di svuotamento gastrico

- Rallenta la peristalsi del piccolo intestino

- Aumenta il rilascio degli enzimi pancreatici

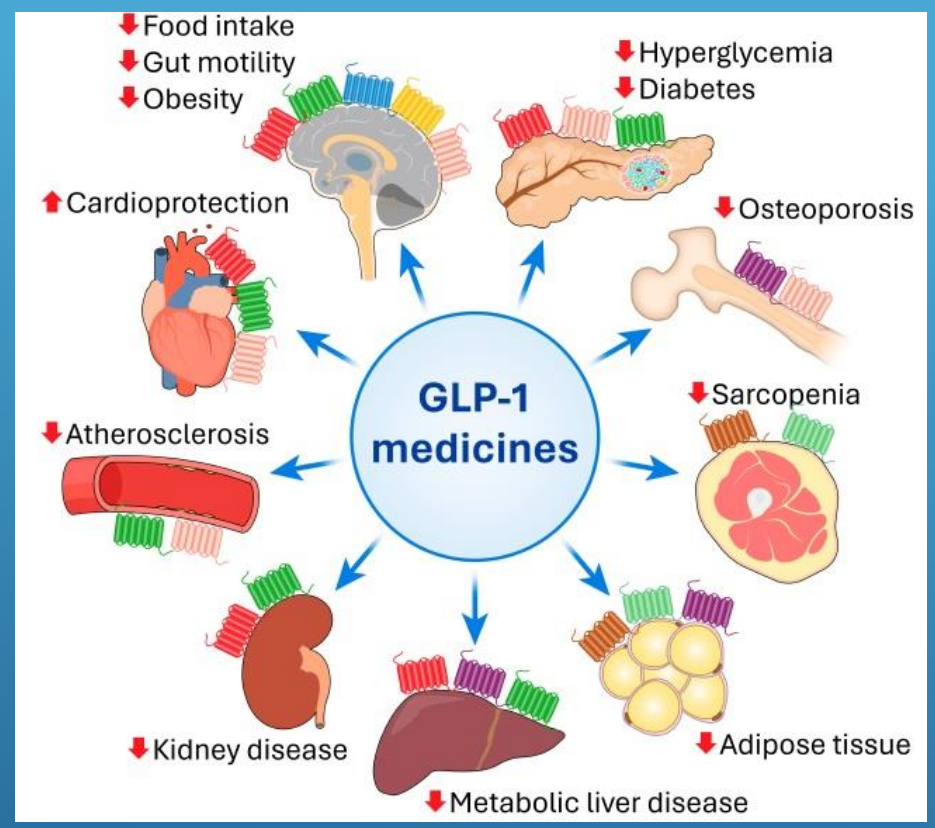
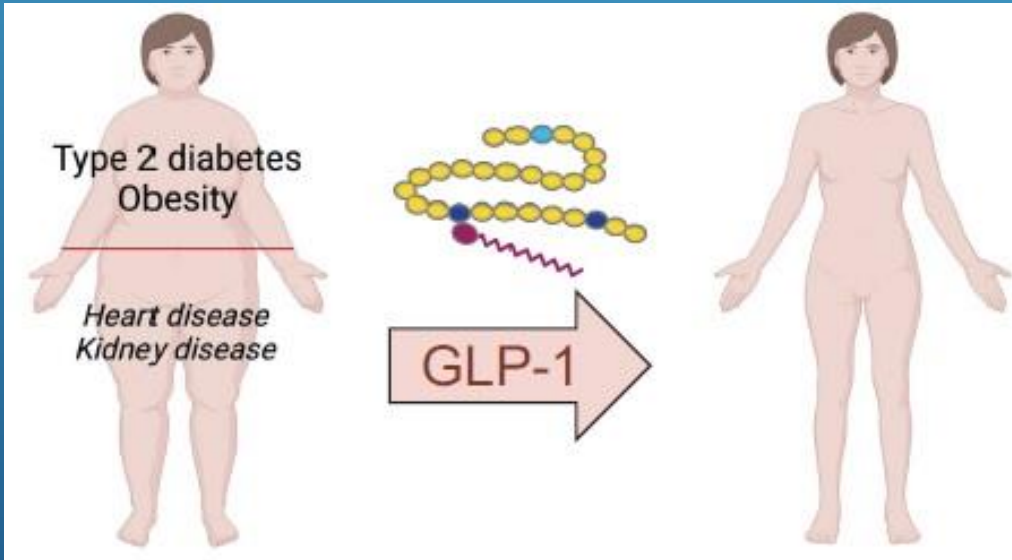
- Incrementa il metabolismo degli adipociti bruni

- Riduce i depositi lipidici negli adipociti bianchi

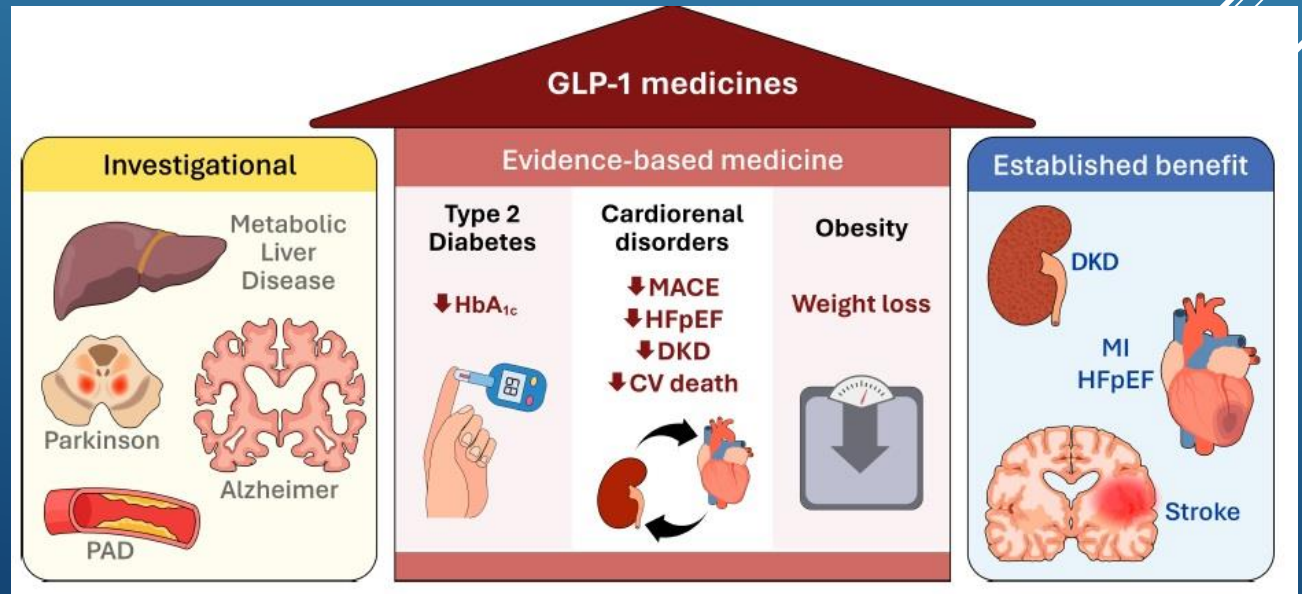
- Favorisce la perdita di peso

Efficacy and Safety of GLP-1 Medicines for Type 2 Diabetes and Obesity

Daniel J. Drucker



GLP1-RA





glp1 weight loss

Advanced Create alert

Save

Email

MY CUSTOM FILTERS

1,923 results

RESULTS BY YEAR



1 Singh G, Krautha
Cite J Investig Med. 2
PMID: 34706925
Share Glucagon-like pe
shown promise i
type 2 diabetes.



glp1 weight loss

Advanced Create alert

Save

Email

MY CUSTOM FILTERS

669 results

RESULTS BY YEAR



1 A GIPR antag
improved me
Cite Véniant MM, Lu
VA, Ambhaikar M
Strande JL.
Share Nat Metab. 2024
PMID: 38316982

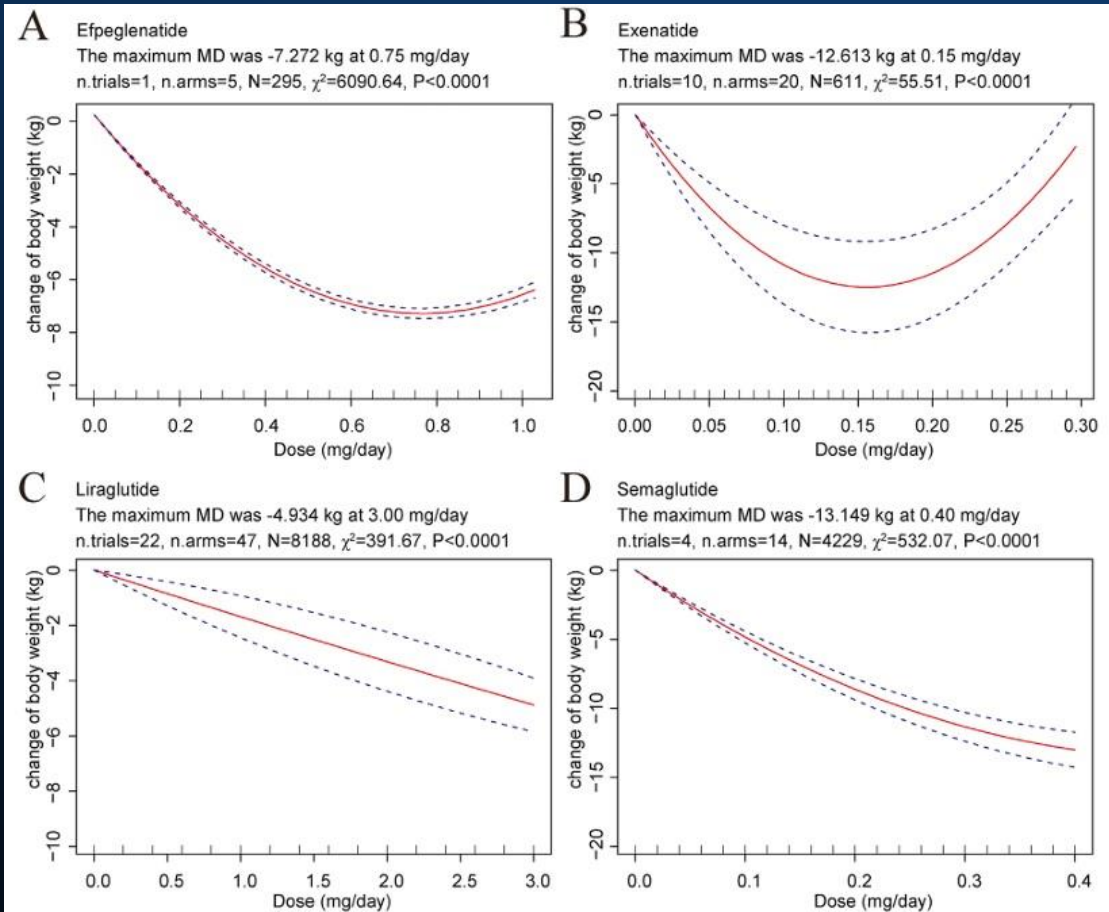


journal homepage: <https://ajcn.nutrition.org/>



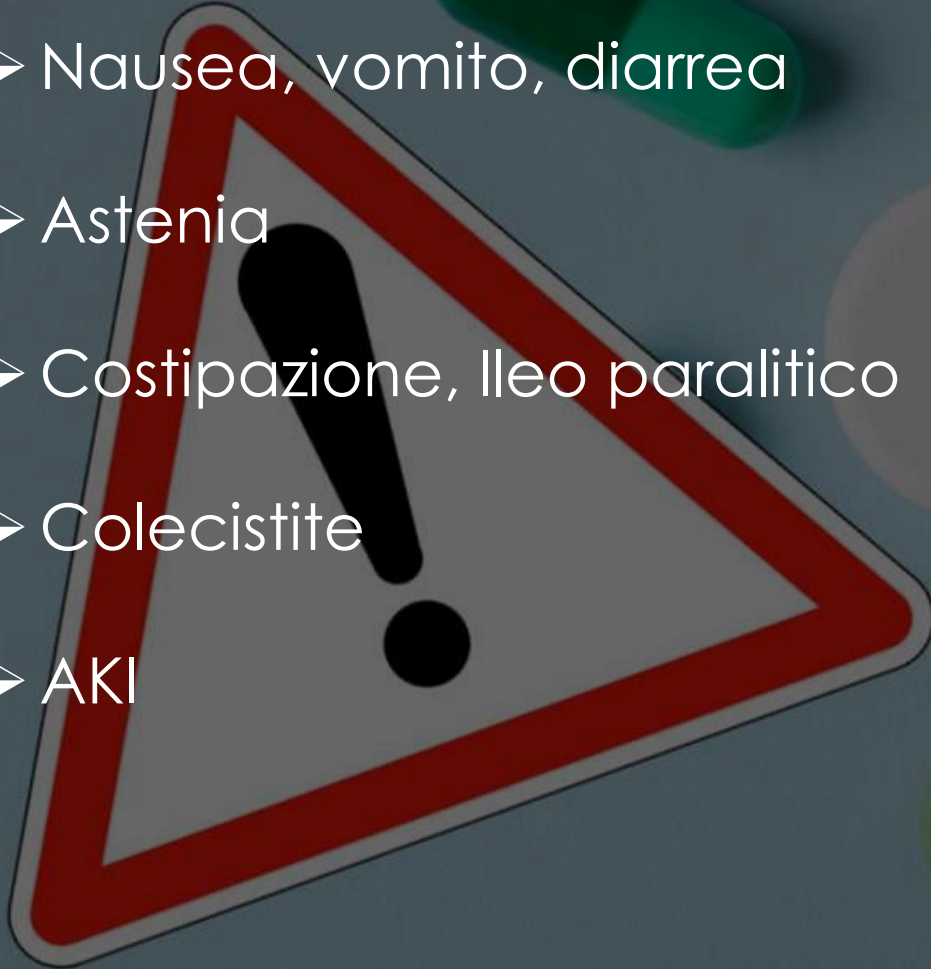
Original Research Article

The Weight-loss Effect of GLP-1RAs Glucagon-Like Peptide-1 Receptor Agonists in Non-diabetic Individuals with Overweight or Obesity: A Systematic Review with Meta-Analysis and Trial Sequential Analysis of Randomized Controlled Trials



EFFETTI INDESIDERATI

- Nausea, vomito, diarrea
- Astenia
- Costipazione, Ileo paralitico
- Colecistite
- AKI



GLP-1RA

INCRETINO-MIMETICI

- *Short-acting*
- Alto potere immunogeno
- Riducono glicemia post-prandiale
- Eliminazione per via renale

ANALOGHI DEL GLP-1 UMANO

- *Long-acting*
- Basso potere immunogeno
- Riducono HbA1c e glicemia a digiuno
- Eliminazione per degradazione proteolitica

Exenatide

5-10 mcg x 2/die

SC

Lixisenatide

10-20 mcg/die

SC

Exenatide LAR

2 mg alla settimana

SC

Dulaglutide

0,75 - 1,5 mg
1 volta a settimana

SC

Semaglutide

0,25 - 0,5 - 1 mg
1 volta alla settimana

SC

Liraglutide

0,6 - 1,2 - 1,8 mg
1 volta al giorno

SC

Semaglutide

3 - 7 - 14 mg
1 volta al giorno

OS

eGFR (ml/min/1.73m ²)		90	85	80	75	70	65	60	55	50	45	40	35	30	25	20	15	10	5
Short-acting GLP-1 RAs																			
Exenatide 10 µg sc twice daily	Green										Yellow Caution			Red					
Lixisenatide 20 µg sc once daily	Green													Red					
Long-acting GLP-1 RAs																			
Albiglutide 30-50 mg sc once weekly	Green													Red					
Dulaglutide 0.75-1.5 mg sc once weekly	Green															Red			
Exenatide ER 2 mg sc once weekly	Green													Red					
Liraglutide 1.2-1.8 mg sc once daily	Green															Red			
Semaglutide 0.5-1.0 mg sc once weekly 7-14 mg po once daily	Green															Red			

Open Access

Systematic Review



Safety and Efficacy of GLP-1 Receptor Agonists in Type 2 Diabetes Mellitus with Advanced and End-Stage Kidney Disease: A Systematic Review and Meta-Analysis

by Pajaree Krisanapan^{1,2,3} , Kanokporn Sanpawithayakul^{4,5} , Pattharawin Pattharanitima² , Charat Thongprayoon¹ , Jing Miao¹  , Michael A. Mao⁶  , Supawadee Suppadungsuk^{1,7} , Supawit Tangpanithandee⁷ , Iasmina M. Craici¹  and Wisit Cheungpasitporn^{1,*}  

EFFICACIA:

- Riduzione della glicemia e di HbA1c
- Riduzione del peso corporeo
- Miglioramento degli outcome cardiaci

SICUREZZA:

- Possibile aumento di effetti avversi GI non gravi
- Mancata aderenza alla terapia

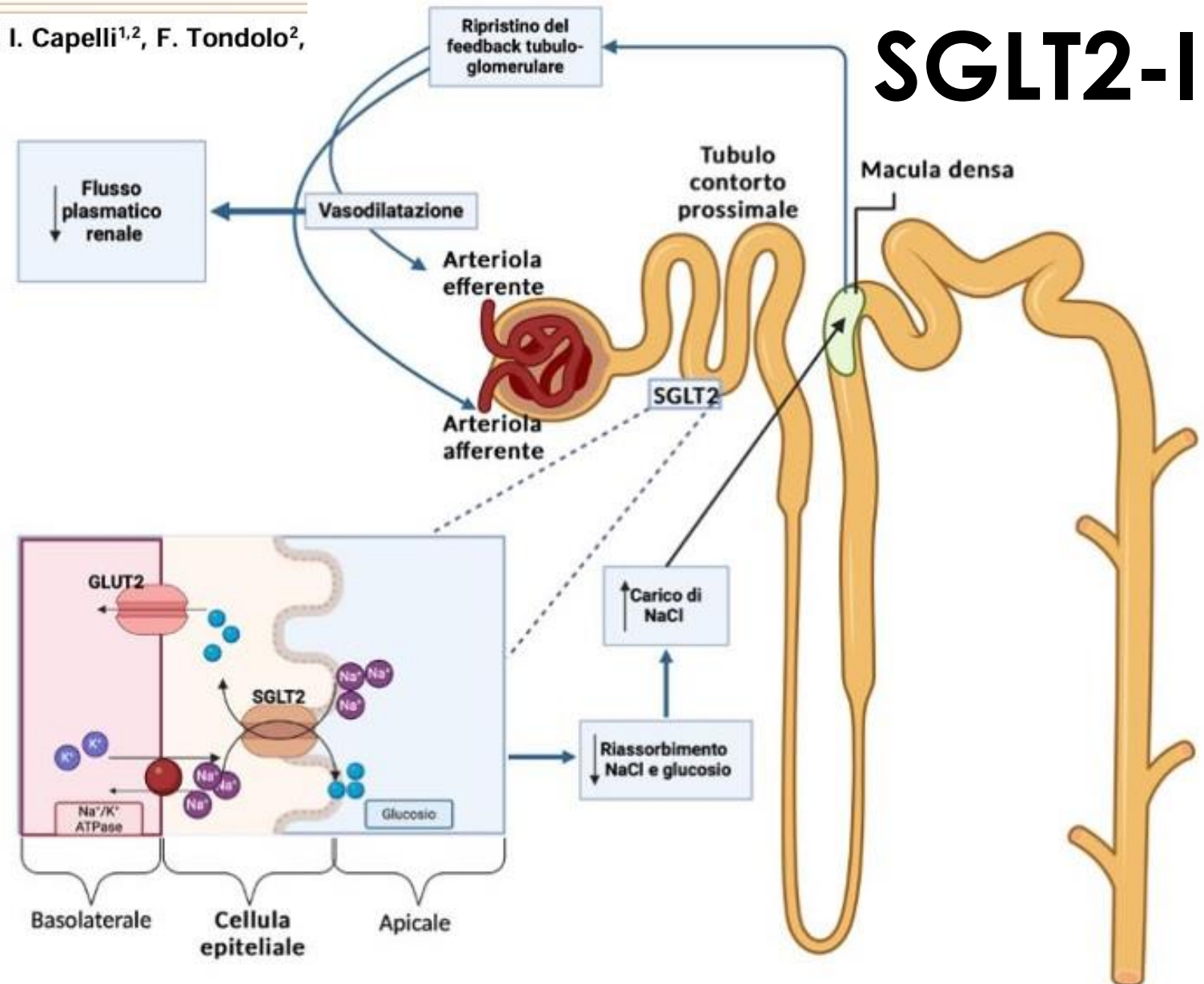
STRETTO MONITORAGGIO DIABETOLOGICO E NEFROLOGICO

Glifozine, contenimento della proteinuria e nefroprotezione

La gestione della malattia renale cronica: vecchi e nuovi approcci

S. Barbuto¹, V. Catalano¹, M. Pira¹, G. Cianciolo², G. Comai^{1,2}, I. Capelli^{1,2}, F. Tondolo², F. Maritati², G. La Manna^{1,2}

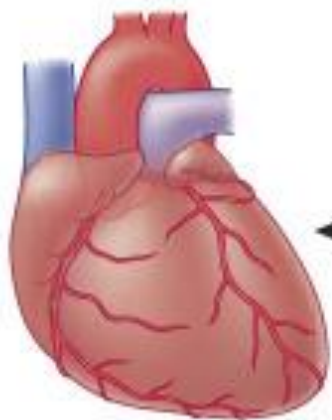
- Inibizione cotrasportatore SGLT2
- Riduzione glucosio in cellule glomerulari e tubuli
- Riduzione prodotti di glicazione avanzata
- Riduzione soglia renale di escrezione del glucosio (180 → 40 mg/dl)
- Riduzione glucotossicità, improvement funzionale cellule β
- Ripristino del feedback tubulo glomerulare
- Natriuresi



Recent results in diabetic and nondiabetic experimental acute myocardial infarction disease models

- ↓ Cardiomyocyte NHE-1
- ↑ Mitochondrial Ca²⁺
- ↓ Transient SGLT2 expression in ischemic heart
- ↓ Adverse remodeling
- ↓ Left ventricular mass
- ↑ Filling conditions

Possible direct cardiac protection

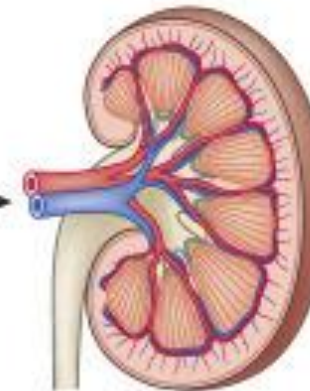


Cardiovascular protection

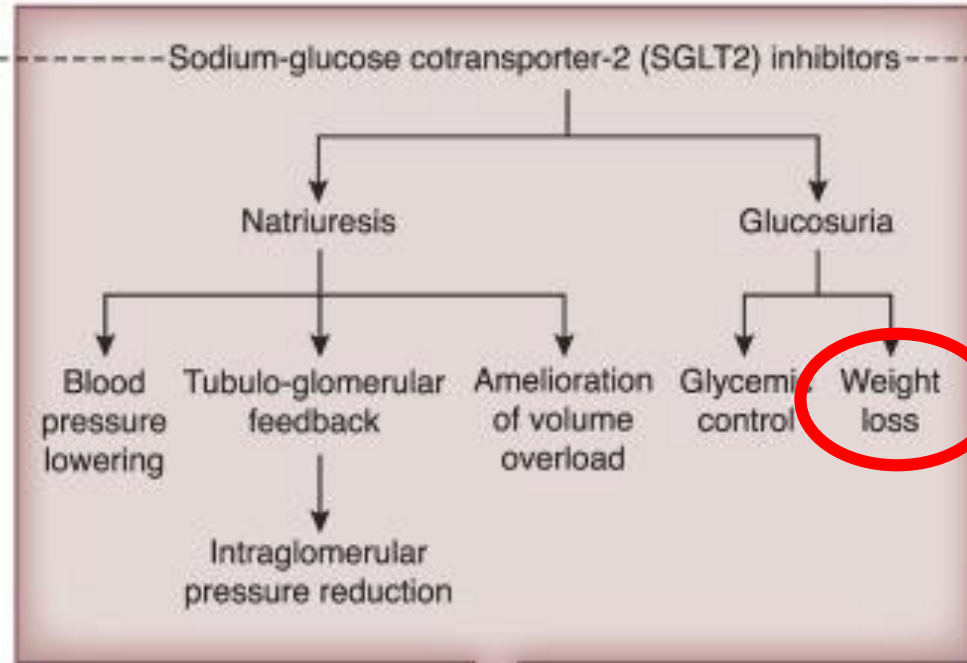
Recent results in nondiabetic experimental chronic kidney disease models

- ↓ Oxidative stress
- ↓ Fibrosis induction
- ↓ Local inflammation
- ↓ Tubular senescence
- ↓ Glomerular damage

Possible direct kidney protection



Kidney protection



Tubular SGLT2 related effects

Generic name
Canagliflozin
Dapagliflozin
Empagliflozin

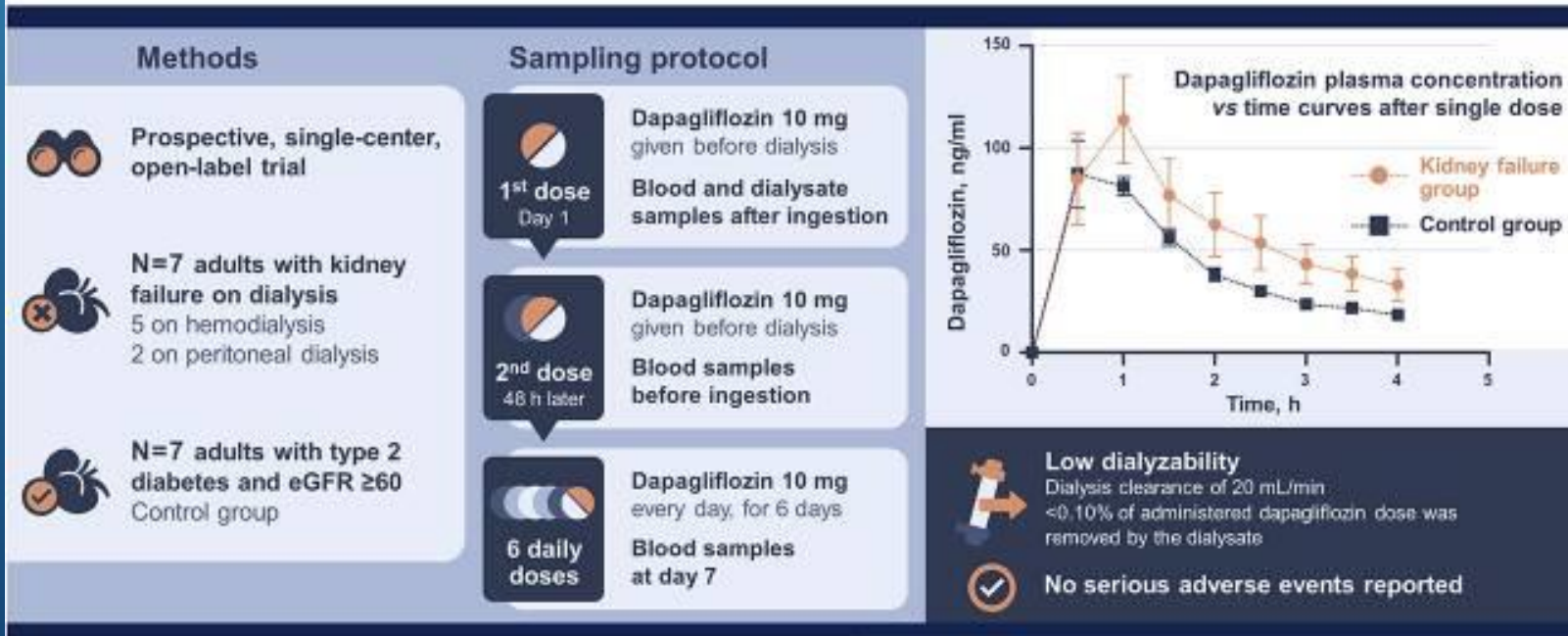
- 
- ▶ Infezioni urinarie e genitali (comprese infezioni micotiche)
 - ▶ Effetto natriuretico e diuretico e transitoria riduzione della funzione renale
 - ▶ Chetoacidosi (rara)
 - ▶ Ipoglicemia
 - ▶ Nausea
 - ▶ Dislipidemia

POSSIBILI EFFETTI AVVERSI

	Stage 3b (eGFR 30-44)	Stage 4 (eGFR 15-29)	Stage 5 (eGFR <15)
Canagliflozin	Maximum 100 mg daily	<ul style="list-style-type: none"> Initiation not recommended May continue 100 mg daily if tolerated for kidney and CV benefit until dialysis 	
Dapagliflozin	10 mg daily [†]	<ul style="list-style-type: none"> Initiation not recommended with eGFR <25 mL/min/1.73 m² May continue if tolerated for kidney and CV benefit until dialysis 	
Empagliflozin	No dose adjustment required	Use for glycemic control not recommended with eGFR <30 mL/min/1.73m ² ; Use recommended with eGFR ≥20 mL/min/1.73m ² to improve CV outcomes in patients with HF	

What are the pharmacokinetic properties of dapagliflozin in hemodialysis and peritoneal dialysis patients?

CJASN
Clinical Journal of the American Society of Nephrology



Conclusions: In individuals with kidney failure on dialysis, dapagliflozin was well-tolerated, was slightly dialyzable, and had nonaccumulating favorable pharmacokinetic properties.

Joaquim Barreto, Cynthia Borges, Tais Betoni Rodrigues, et al.
Pharmacokinetic Properties of Dapagliflozin in Hemodialysis and Peritoneal Dialysis Patients. CJASN doi: 10.2215/CJN.000000000000196.
 Visual Abstract by Corina-Gabriela Teodosiu, MD

SGLT2 Inhibition in Hemodialysis (DAPA-HD)

ClinicalTrials.gov ID ⓘ NCT05179668

Sponsor ⓘ Medical University of Vienna

Information provided by ⓘ Assoc. Prof. Dr. Manfred Hecking, MD PhD, Medical University of Vienna (Responsible Party)

Last Update Posted ⓘ 2022-10-25

Valutazione degli outcome cardiaci in ESRD

The RENAL LIFECYCLE Trial: A RCT to Assess the Effect of Dapagliflozin on Renal and Cardiovascular Outcomes in Patients With Severe CKD

ClinicalTrials.gov ID ⓘ NCT05374291

Sponsor ⓘ University Medical Center Groningen

Information provided by ⓘ Ron Gansevoort, University Medical Center Groningen (Responsible Party)

Last Update Posted ⓘ 2024-06-03

Valutazione cardio e nefroprotezione in:

- **CKD avanzata (eGFR < 25 ml/min)**
- **ESRD un trattamento sostitutivo (diuresi residua 500 cc/die)**
- **Portatori di graft renale con eGFR < 45 ml/min**

Obesità FdR per progressione CKD

Limitazioni al trapianto

Terapia farmacologica: GLP1-RA e SGLT2-i

GLP1-RA utilizzabili off-label in ESRD, nonostante efficacia e sicurezza

Possibili *Side Effects* non gravi

SGLT2-i non attualmente utilizzabili in ESRD

Trial per uso di SGLT2-i in ESRD



Sale Dialisi



GRAZIE PER
L'ATTENZIONE