



SGLT-2 inibitori: il punto di vista del Nefrologo

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Agenda



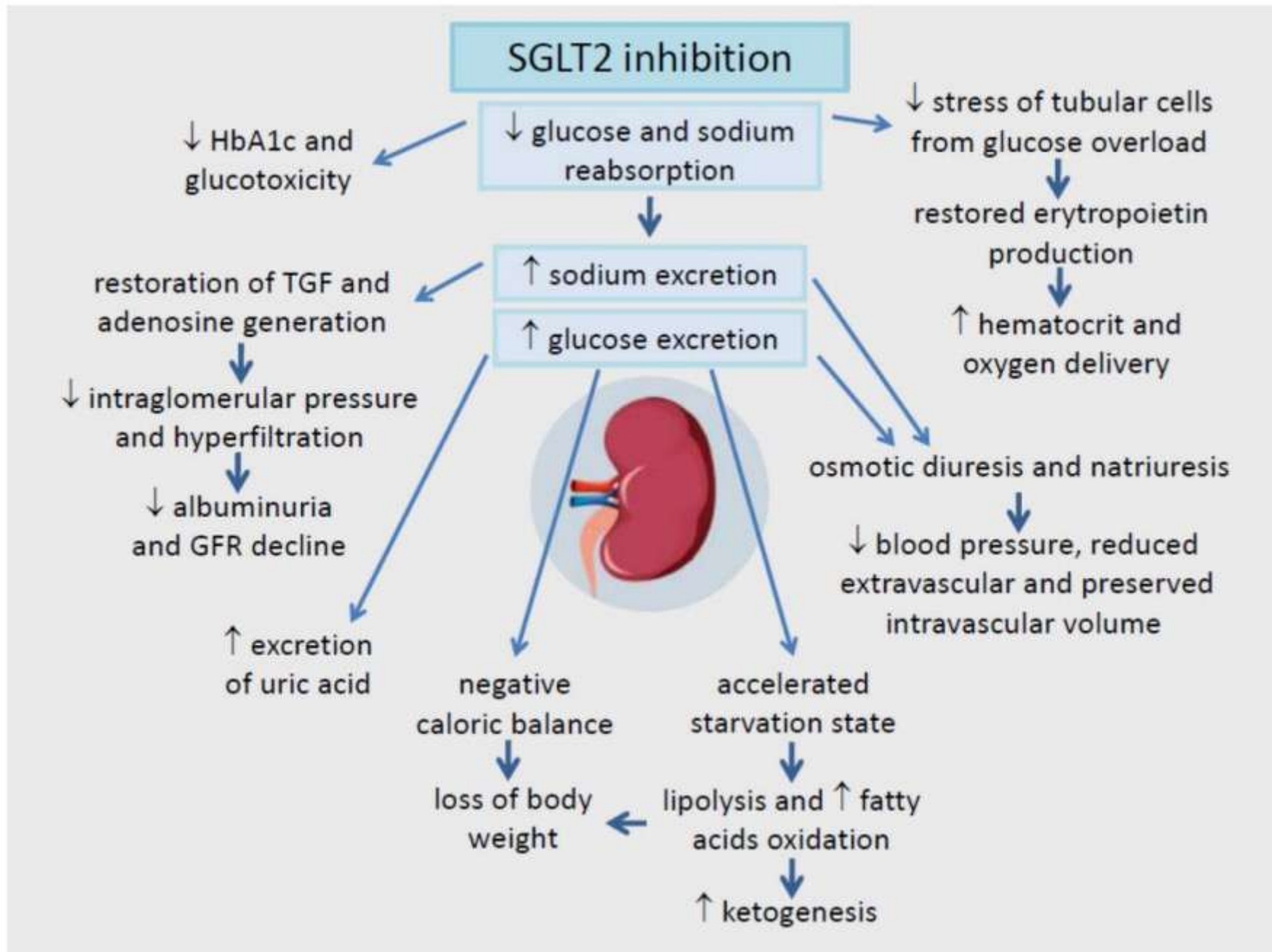
LA FISIOPATOLOGIA
RENALE DEGLI SGLT2I



LE EVIDENZE
«NEFROLOGICHE»



LA PRESCRIVIBILITÀ IN
RELAZIONE AL GFR

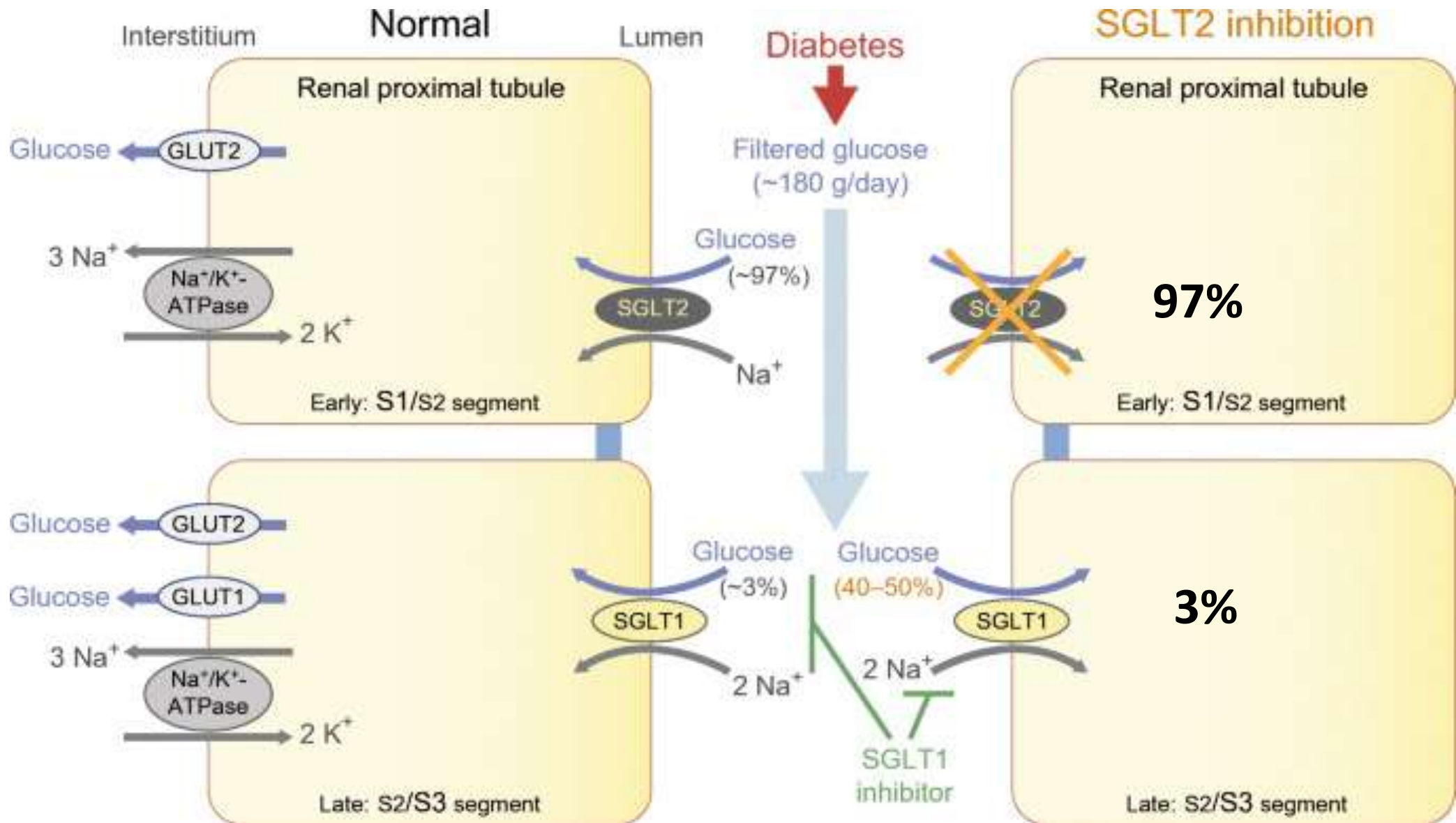


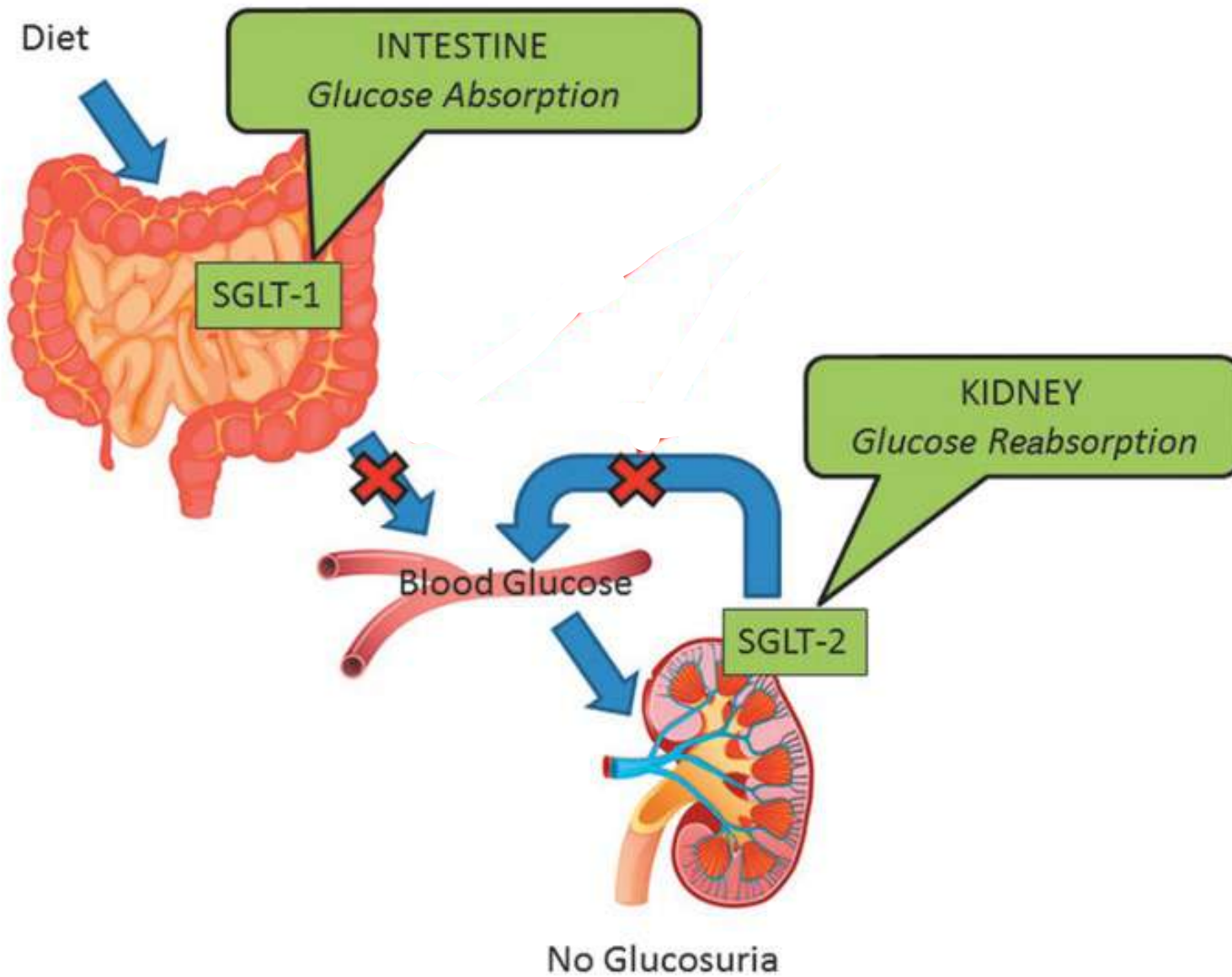


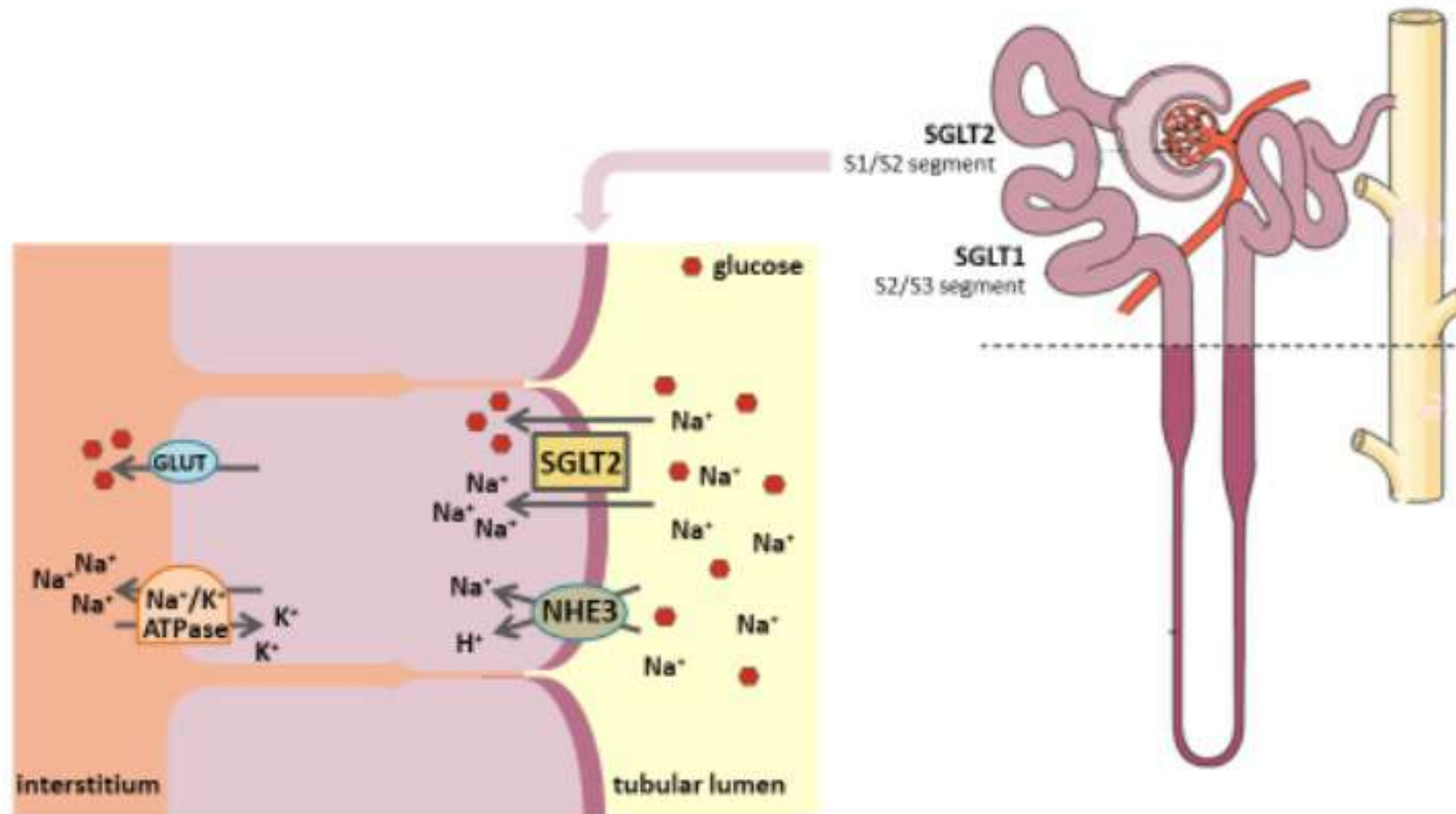
Conclusioni - I

- La fisiopatologia della nefroprotezione (proteinuria, iperfiltrazione, sovraccarico di volume, chetogenesi, dimagrimento, uricuria, stress tubulare)





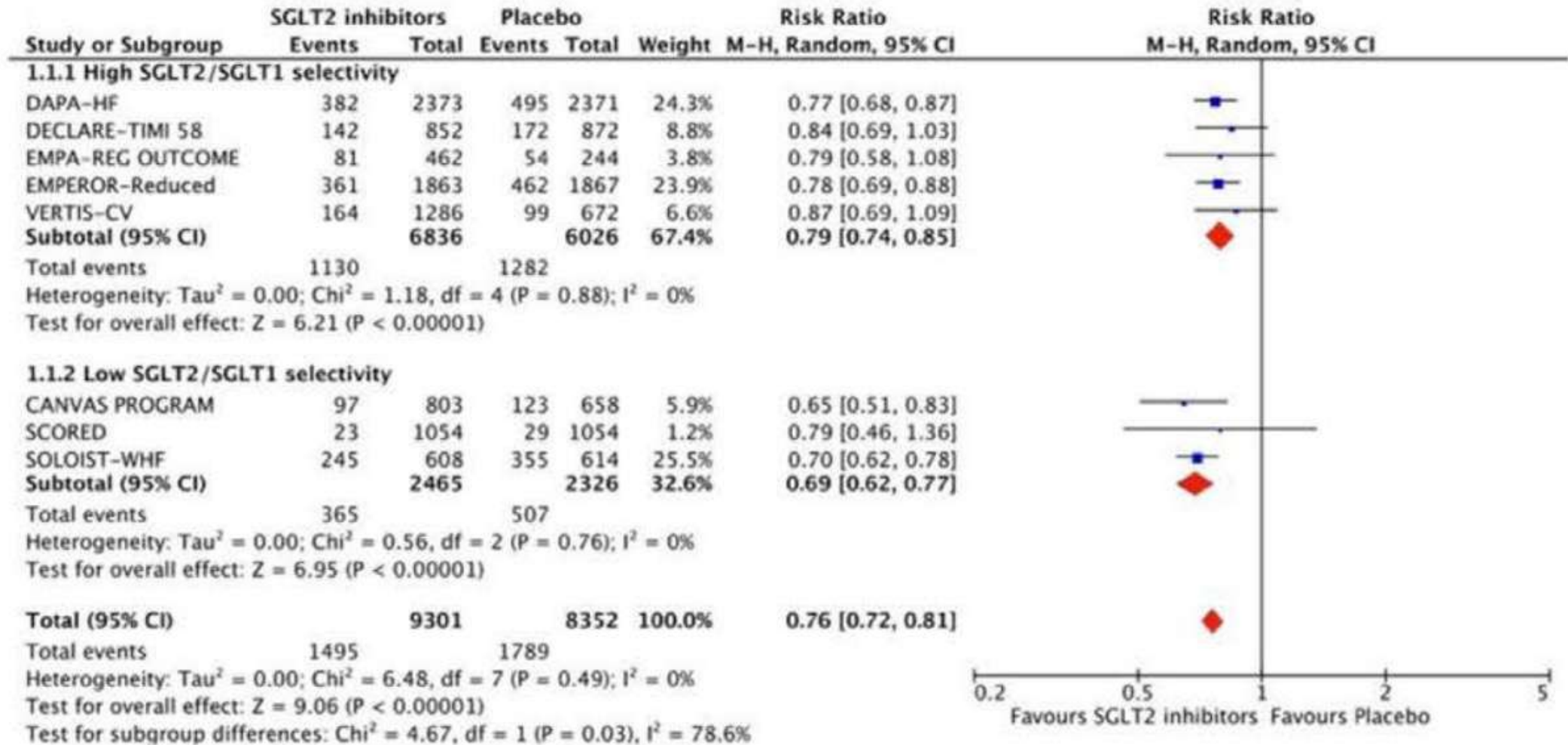




SGLT-I	EMA approval	Selectivity SGLT2 vs SGLT1	Dosage (mg)	Half-life (T/2)
Dapagliflozin	2012	>1400 - fold	5 - 10 mg	13 h
Canagliflozin	2013	~ 250 fold	100 - 300 mg	11 - 13 h
Empagliflozin	2014	>2500 - fold	10 - 25 mg	13 h
Ertugliflozin	2017	~ 2000 - fold	5 - 15 mg	16.6 h

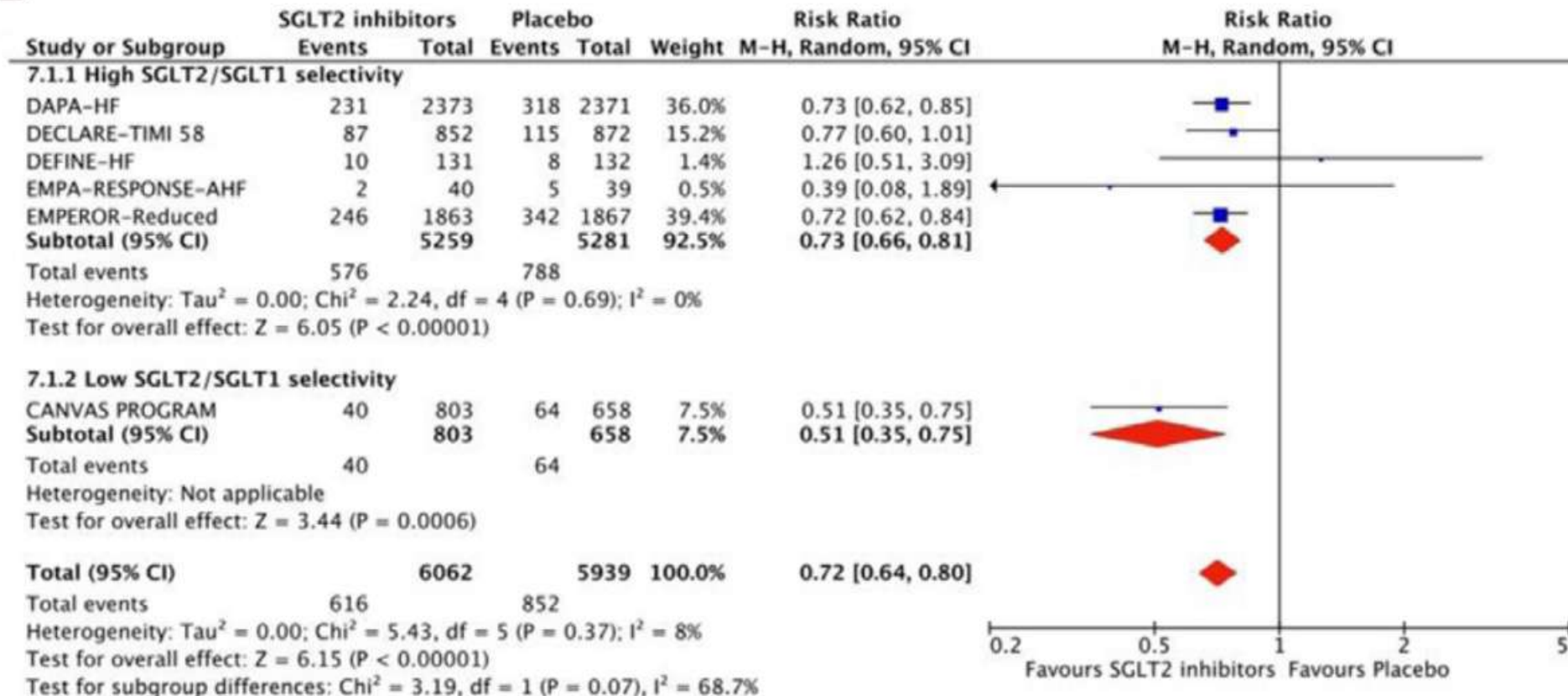
Mortalità cardiovascolare ed ospedalizzazione per scompenso (dati stratificati per alta o bassa selettività)

B



Ospedalizzazione per scompenso (dati stratificati per alta o bassa selettività)

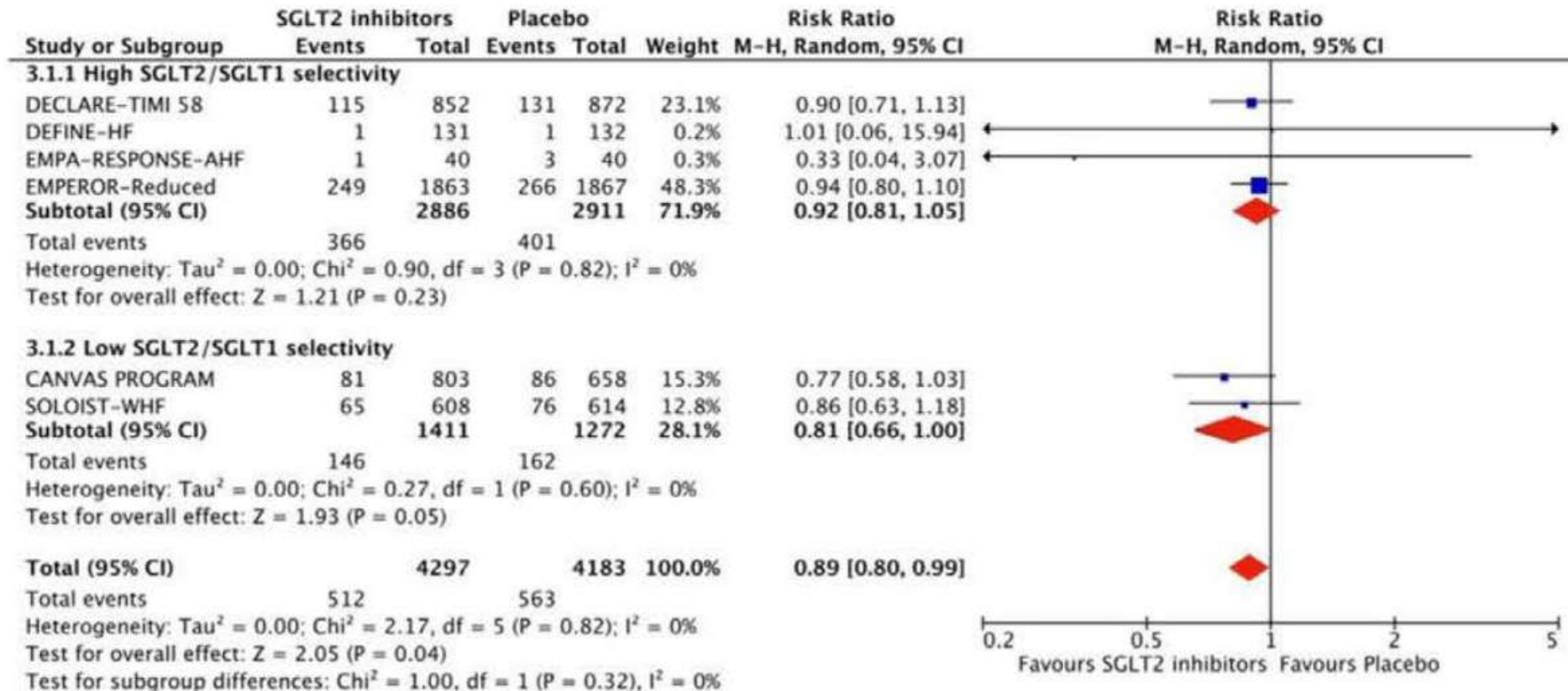
B

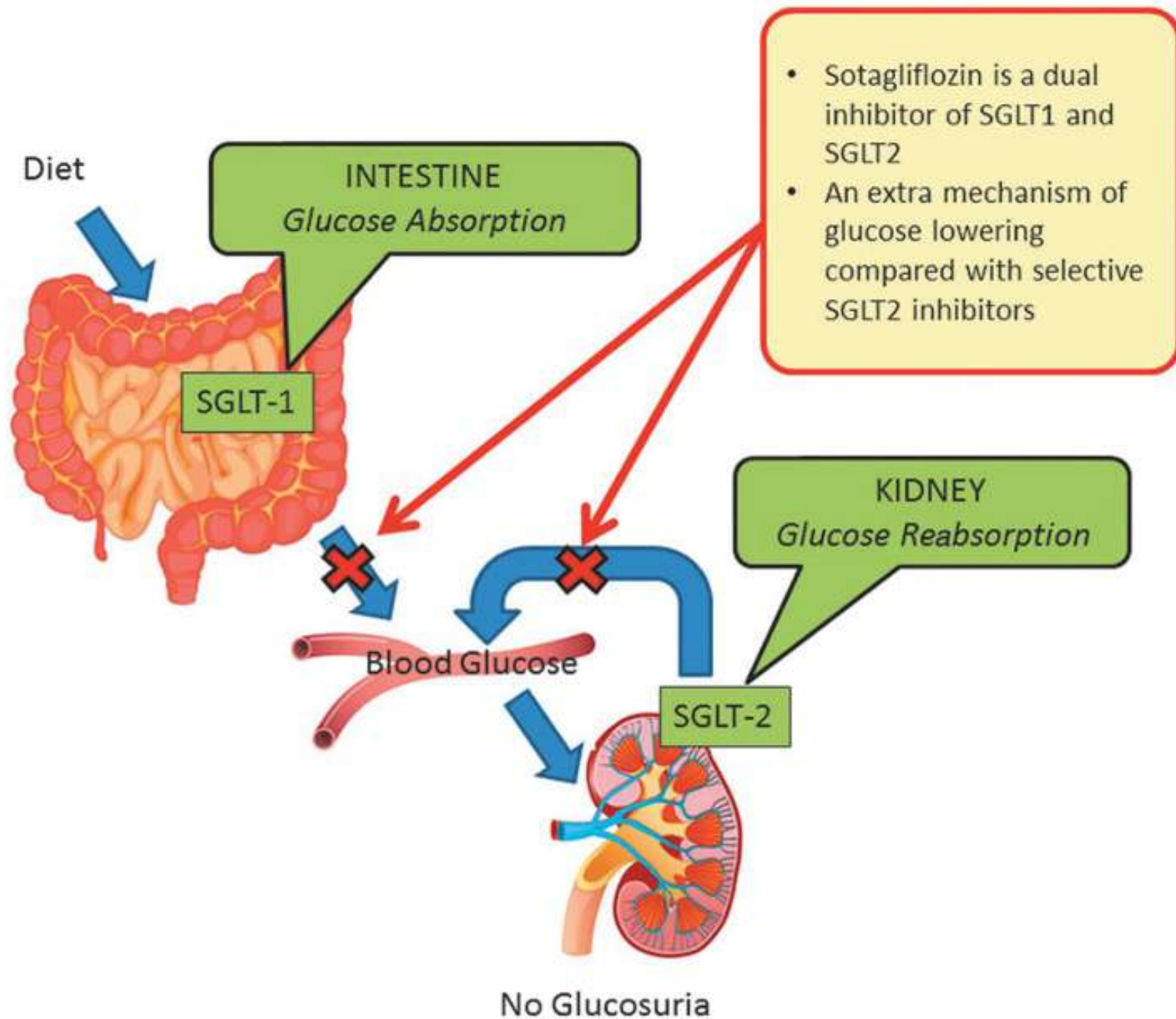


Mortalità totale

(dati stratificati per alta o bassa selettività)

B





Conclusioni - II

- La fisiopatologia della nefroprotezione (proteinuria, iperfiltrazione, sovraccarico di volume, chetogenesi, dimagrimento, uricuria, stress tubulare)
- La selettività per SGLT2/SGLT1

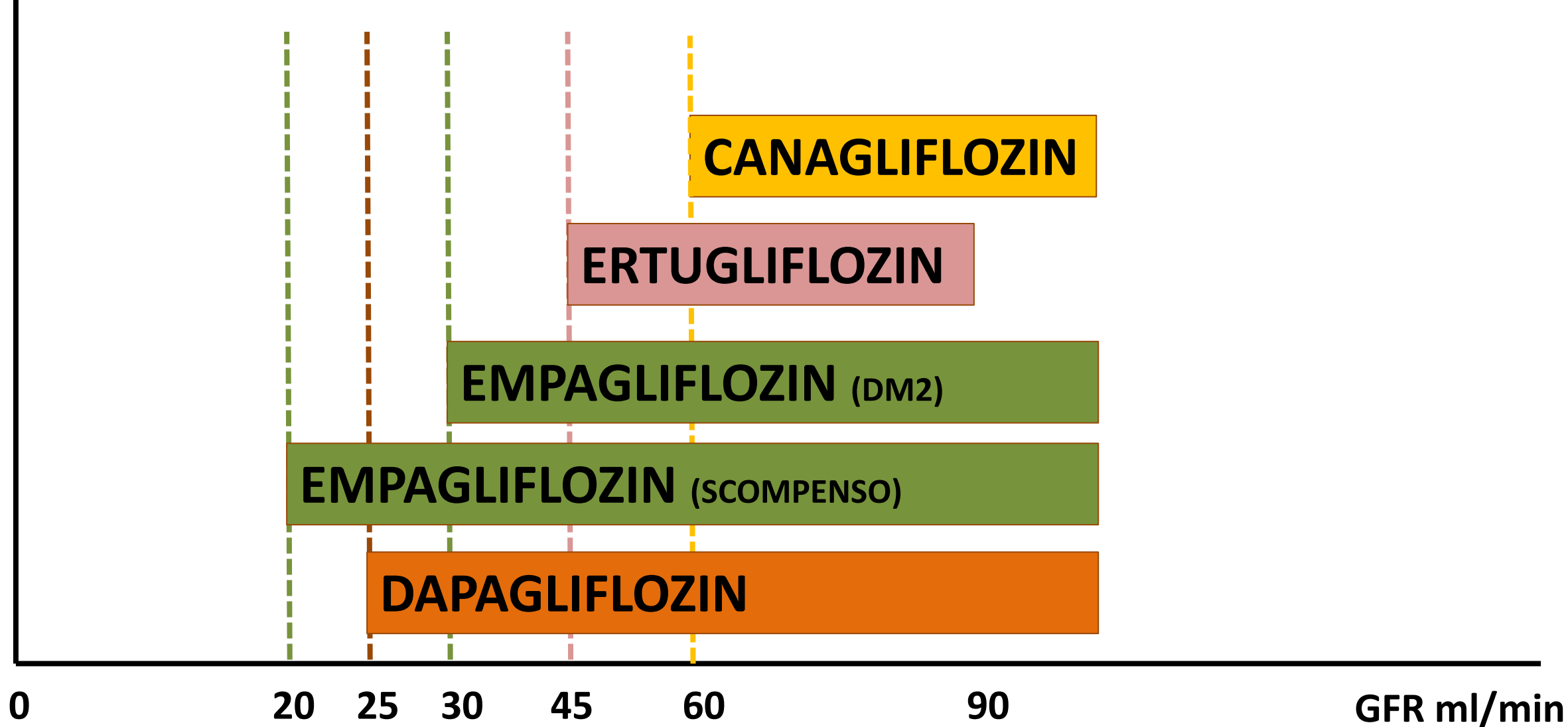




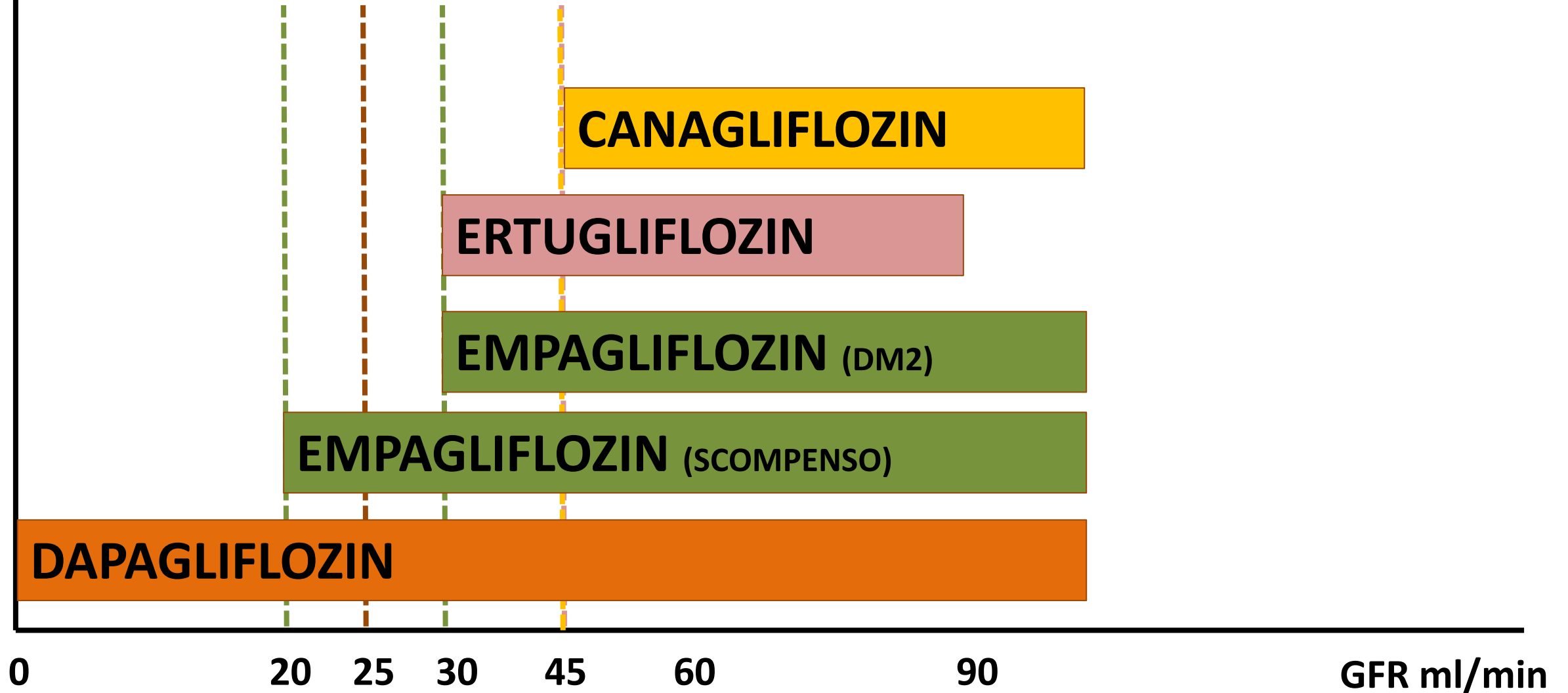
LA PRESCRIVIBILITÀ IN RELAZIONE AL GFR

Signature

L'AVVIO DELLA TERAPIA



L'INTERRUZIONE DELLA TERAPIA



Conclusioni - III

- La **fisiopatologia della nefroprotezione** (proteinuria, iperfiltrazione, sovraccarico di volume, chetogenesi, dimagrimento, uricuria, stress tubulare)
- La **selettività per SGLT2/SGLT1**
- Dapagliflozin ed empagliflozin prescrivibili per GFR più bassi
- Dapagliflozin non necessita di sospensione per GFR





EVIDENZE DI LETTERATURA



- Credence
- DAPA-CKD
- EMPA-KIDNEY



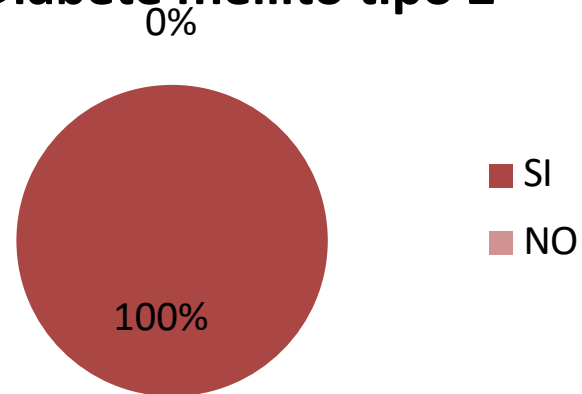
LO STUDIO CREDENCE

Lo studio CREDENCE

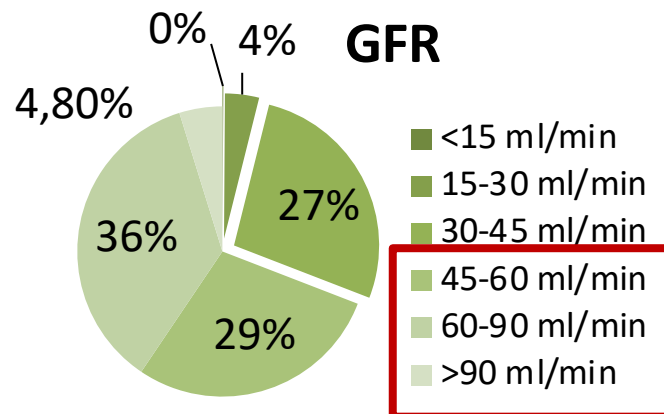
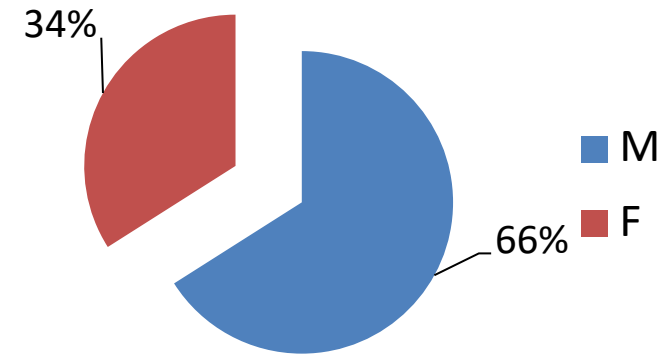
- 4401 pazienti
- DM2, albuminuria
- eGFR 30-90 ml/min ed albuminuria (ACR >300 - 5000)
- Outcome primario: composito di ESRD, raddoppio della creatinina, morte da cause renali o cardiovascolari

Credence: caratteristiche dei pazienti

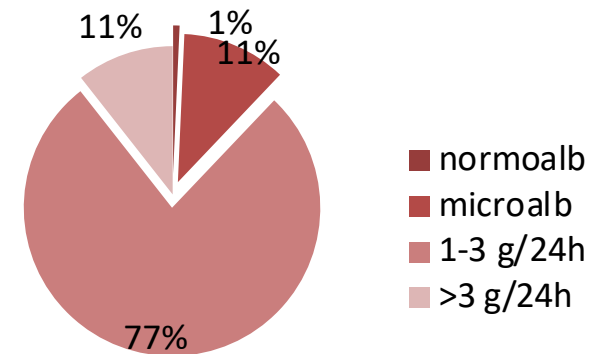
Diabete mellito tipo 2



M vs F

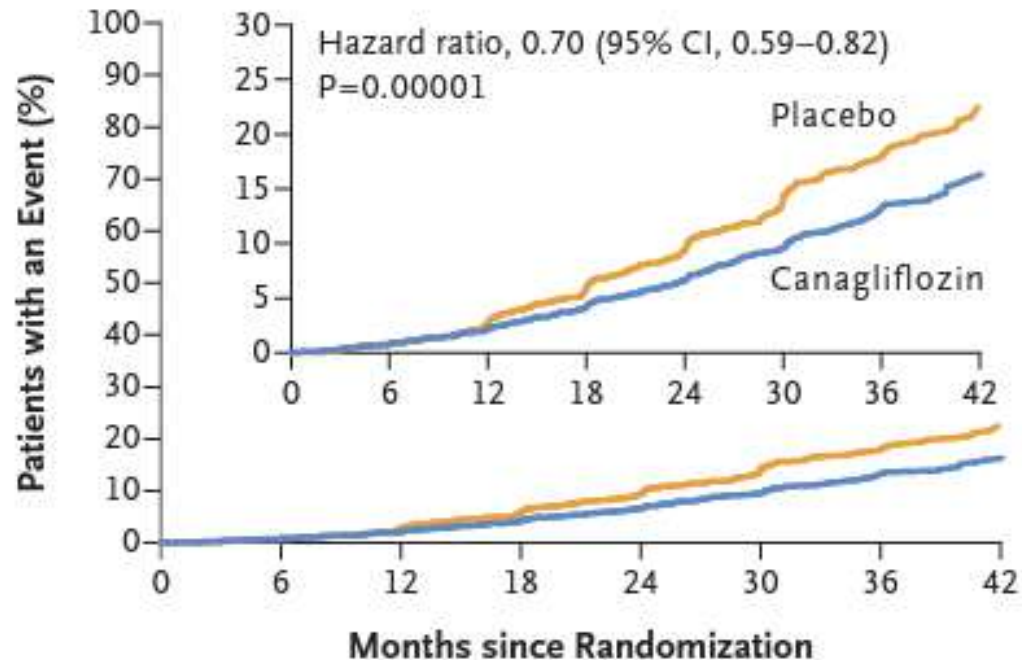


ACR



CREDESCENCE: l'outcome primario

A Primary Composite Outcome



composite of:

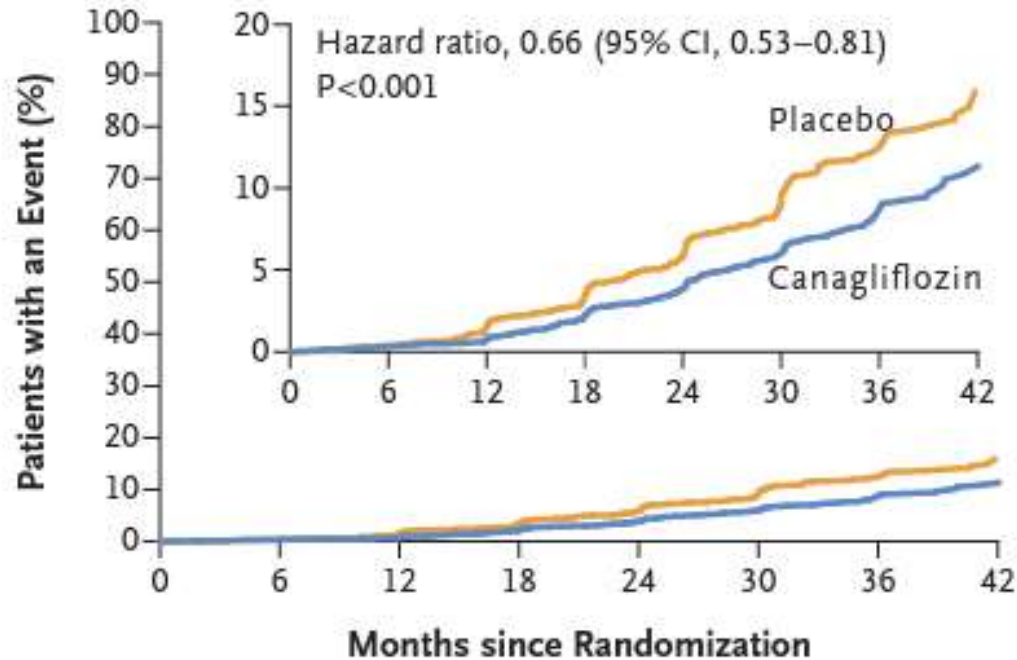
- end-stage kidney disease (dialysis, transplantation, or a sustained eGFR of <15 ml/min,
- a doubling of the serum creatinine level,
- death from renal or cardiovascular causes

No. at Risk

Placebo	2199	2178	2132	2047	1725	1129	621	170
Canagliflozin	2202	2181	2145	2081	1786	1211	646	196

CREDESCENCE: gli outcome renali

B Renal-Specific Composite Outcome



composite of:

- end-stage kidney disease (dialysis, transplantation, or a sustained eGFR of <15 ml/min,
- a doubling of the serum creatinine level,
- death from renal causes

No. at Risk

Placebo	2199	2178	2131	2046	1724	1129	621	170
Canagliflozin	2202	2181	2144	2080	1786	1211	646	196

A photograph of a desk with various items: a notebook with a chemical structure drawing, a yellow highlighter, a stack of colorful sticky notes, and an orange mug. A semi-transparent dark grey box is overlaid on the notebook, containing the text 'LO STUDIO DAPA-CKD'.

LO STUDIO DAPA-CKD

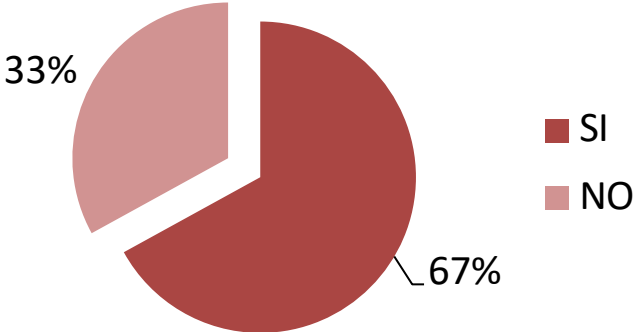
N Engl J Med. 2023 January 12; 388(2): 117–127

Lo studio DAPA-CKD

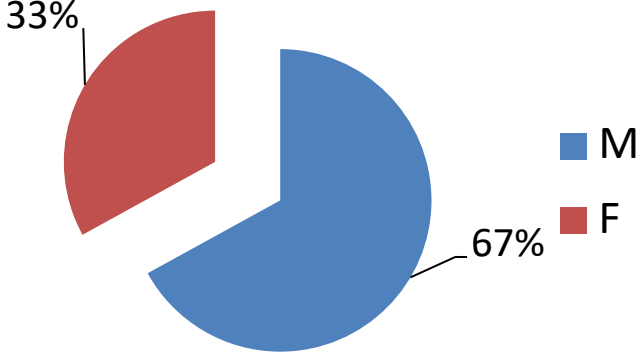
- 4304 pazienti
- DM2 proteinurici e proteinurici non diabetici
- Dapagliflozin (10 mg/die) vs placebo.
- eGFR 25-75 ml/min
- UACR 200-5000 mg/g

DAPACKD: caratteristiche dei pazienti

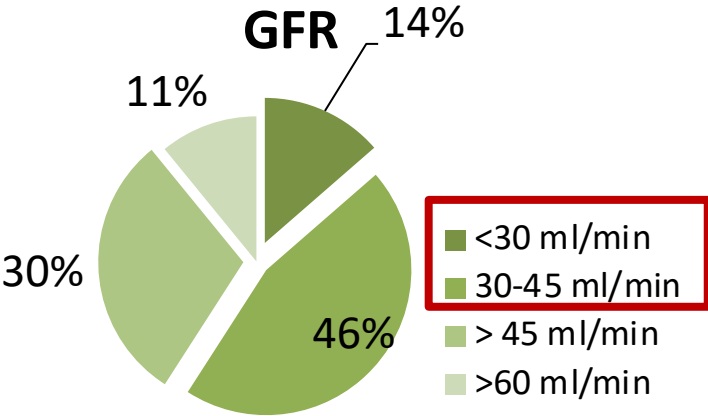
Diabete mellito tipo 2



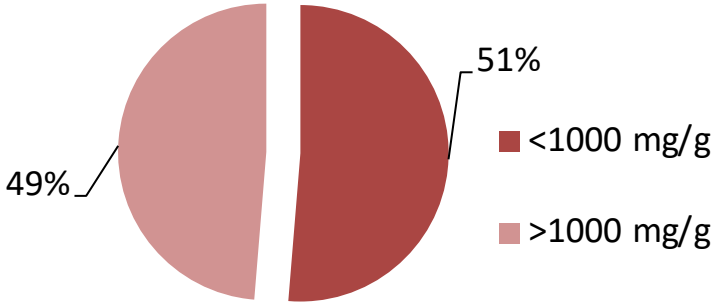
M vs F



GFR

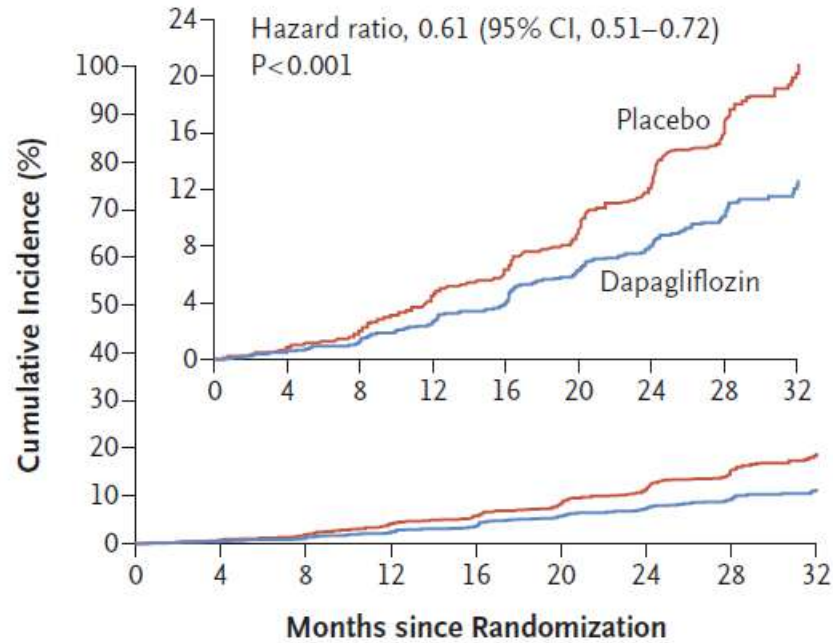


ACR



Dapa-CKD

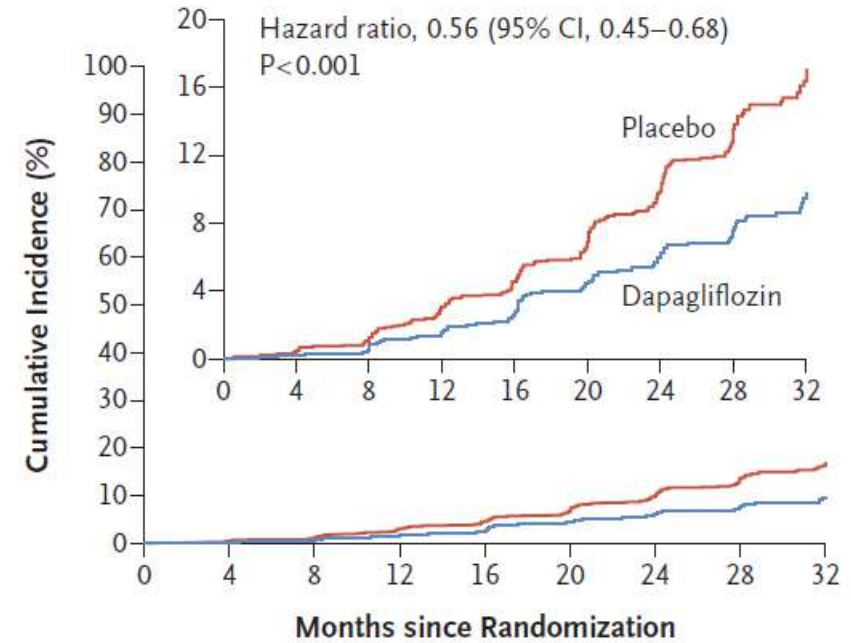
A Primary Composite Outcome



No. at Risk

Placebo	2152	1993	1936	1858	1791	1664	1232	774	270
Dapagliflozin	2152	2001	1955	1898	1841	1701	1288	831	309

B Renal-Specific Composite Outcome



No. at Risk

Placebo	2152	1993	1936	1858	1791	1664	1232	774	270
Dapagliflozin	2152	2001	1955	1898	1841	1701	1288	831	309

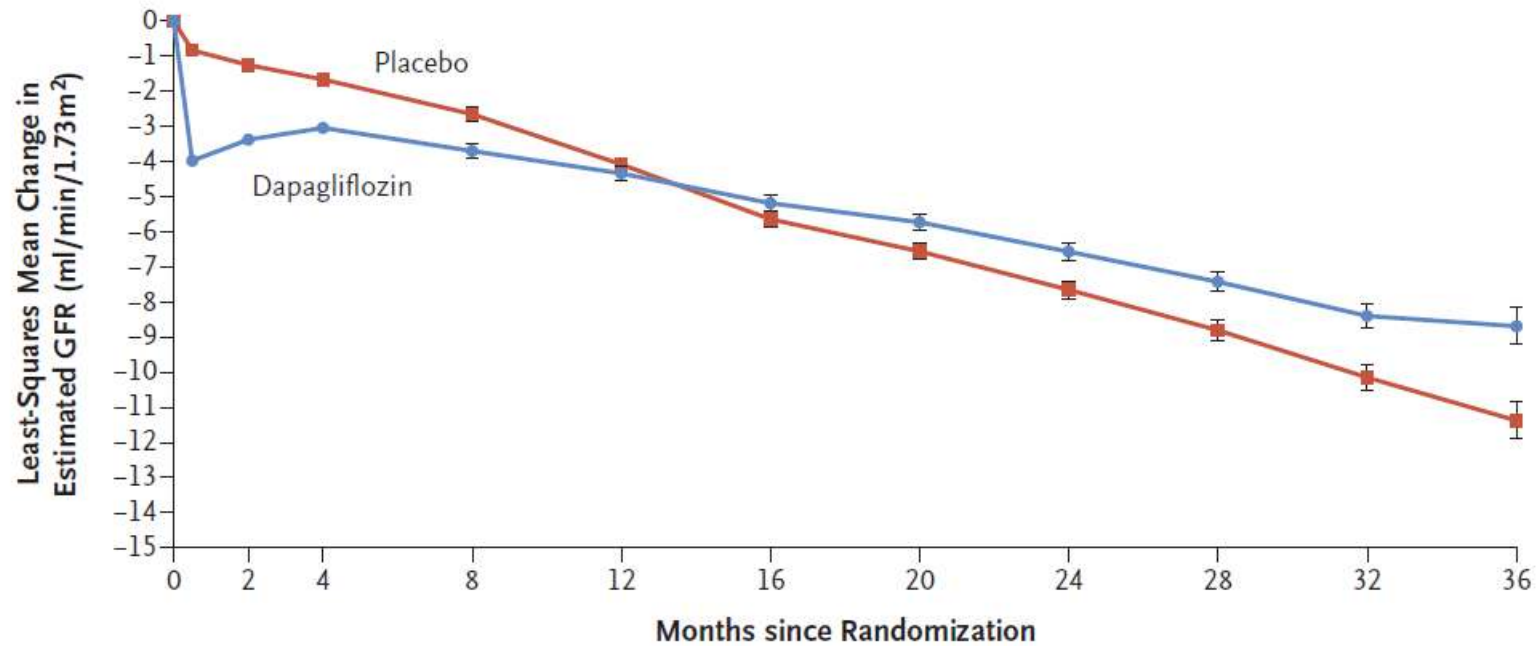
Composito di

- declino del GFR >50%,
- uremia terminale
- morte da cause renali o cardiovascolari

Composito di

- declino del GFR >50%,
- uremia terminale
- morte da cause renali

Dapa-CKD



No. of Participants

Placebo	2152	2029	1981	1866	1795	1753	1672	1443	935	447	157
Dapagliflozin	2152	2031	2001	1896	1832	1785	1705	1482	978	496	157

Figure 3. Change from Baseline in Estimated GFR.

Shown is the least-squares mean change from baseline in the estimated GFR, calculated with the use of a repeated-measures analysis including terms for trial group, baseline measurement, visit, and interaction between visit and trial group. The I bars indicate standard errors. The mean estimated GFR at baseline was 43.2 ml per minute per 1.73 m² of body-surface area in the dapagliflozin group and 43.0 ml per minute per 1.73 m² in the placebo group.

LO STUDIO EMPAKIDNEY

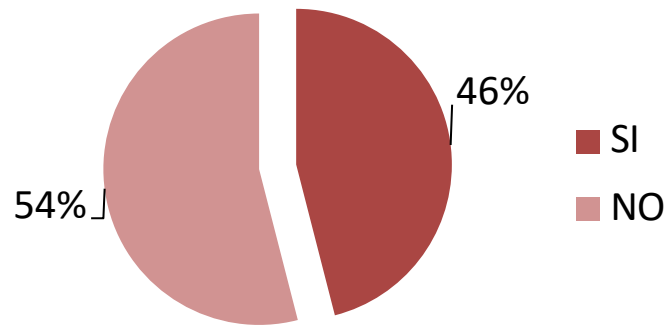
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Lo studio EMPA-KIDNEY

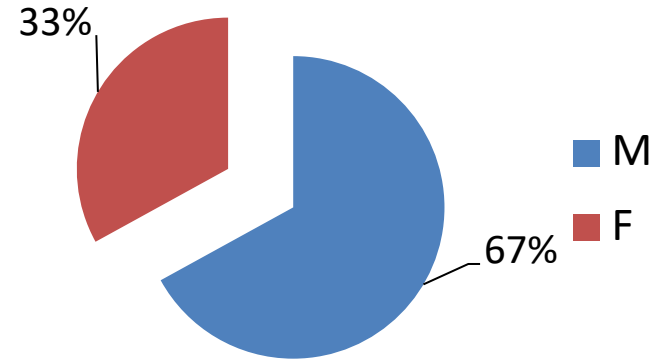
- 6609 pazienti
- Diabetici proteinurici, proteinurici non diabetici
- empagliflozin (10mg/die) vs placebo.
- eGFR tra 20 e 45 ml/min
- eGFR tra 45 e 90 ml/min con microalbuminuria (ACR \geq 200 mg/g)

Caratteristiche dei pazienti

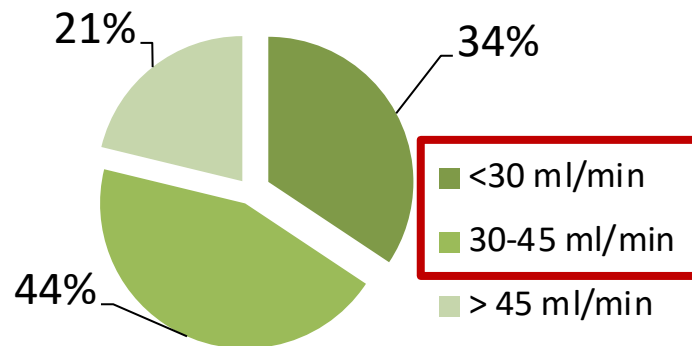
Diabete mellito tipo 2



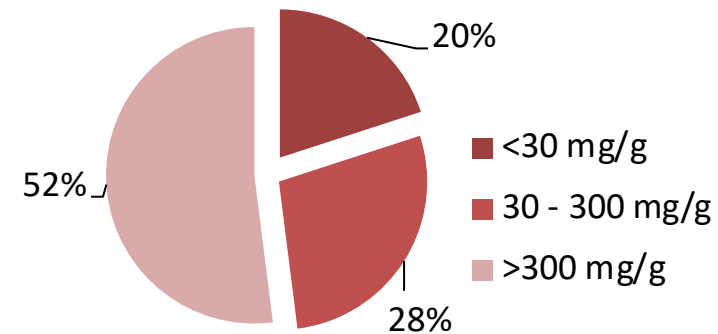
M vs F



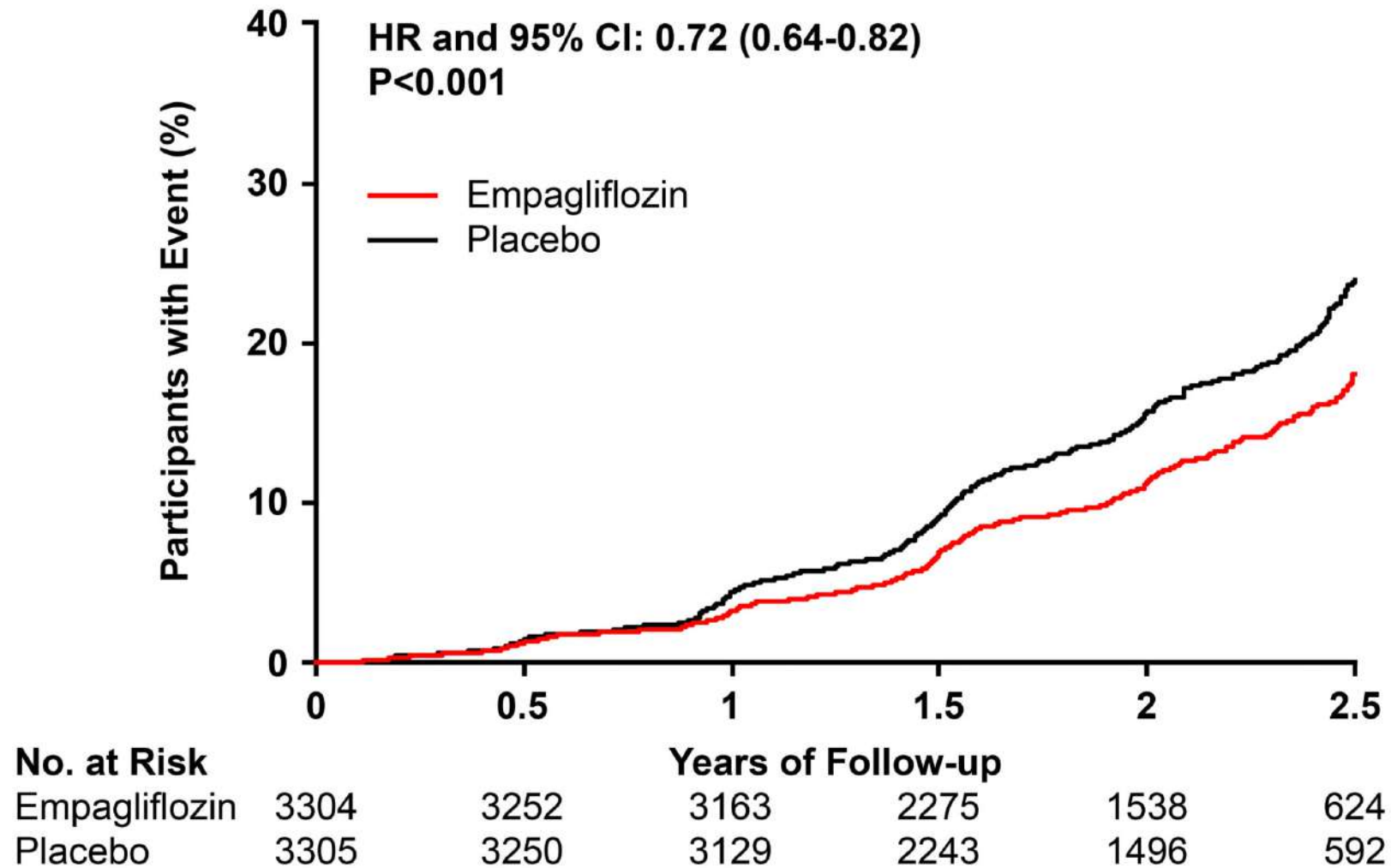
GFR



ACR



Kidney disease progression or death from cardiovascular causes



Empakidney

et al.

Page 13

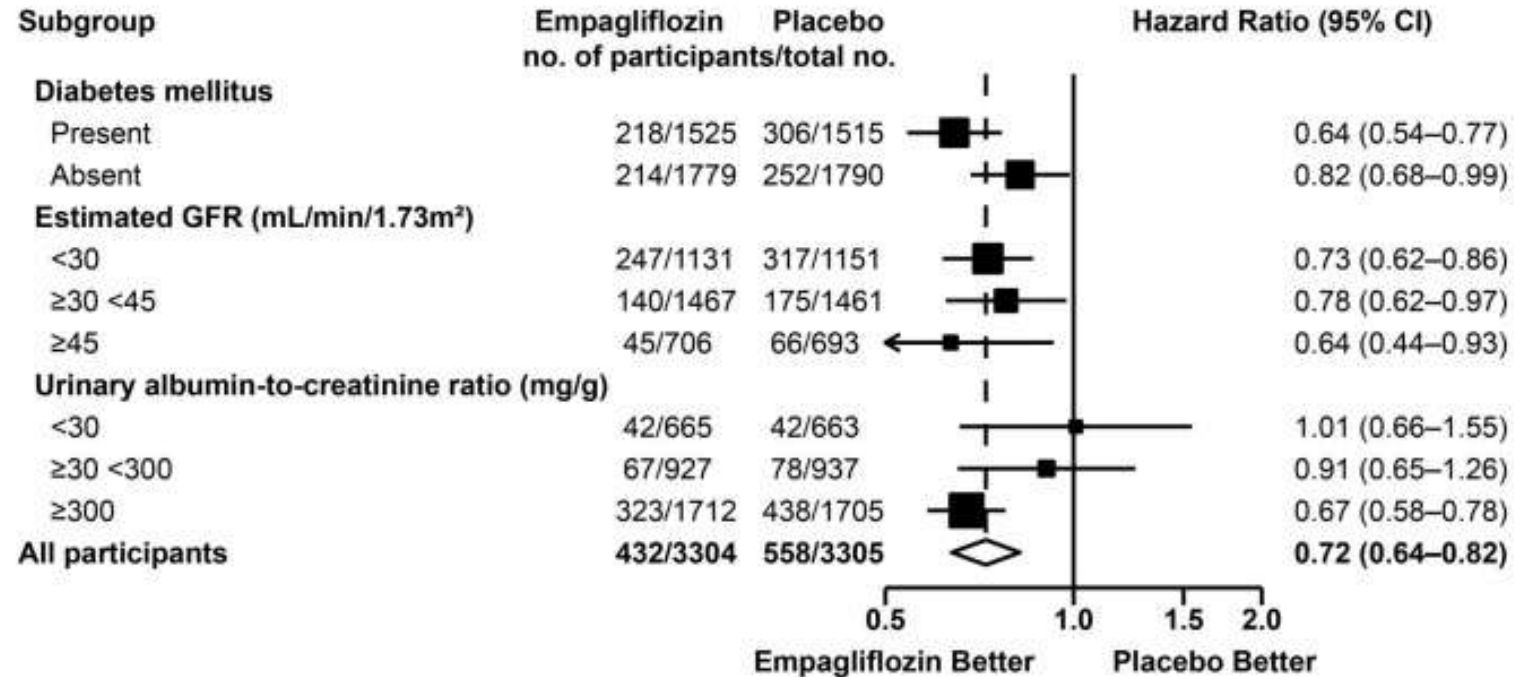


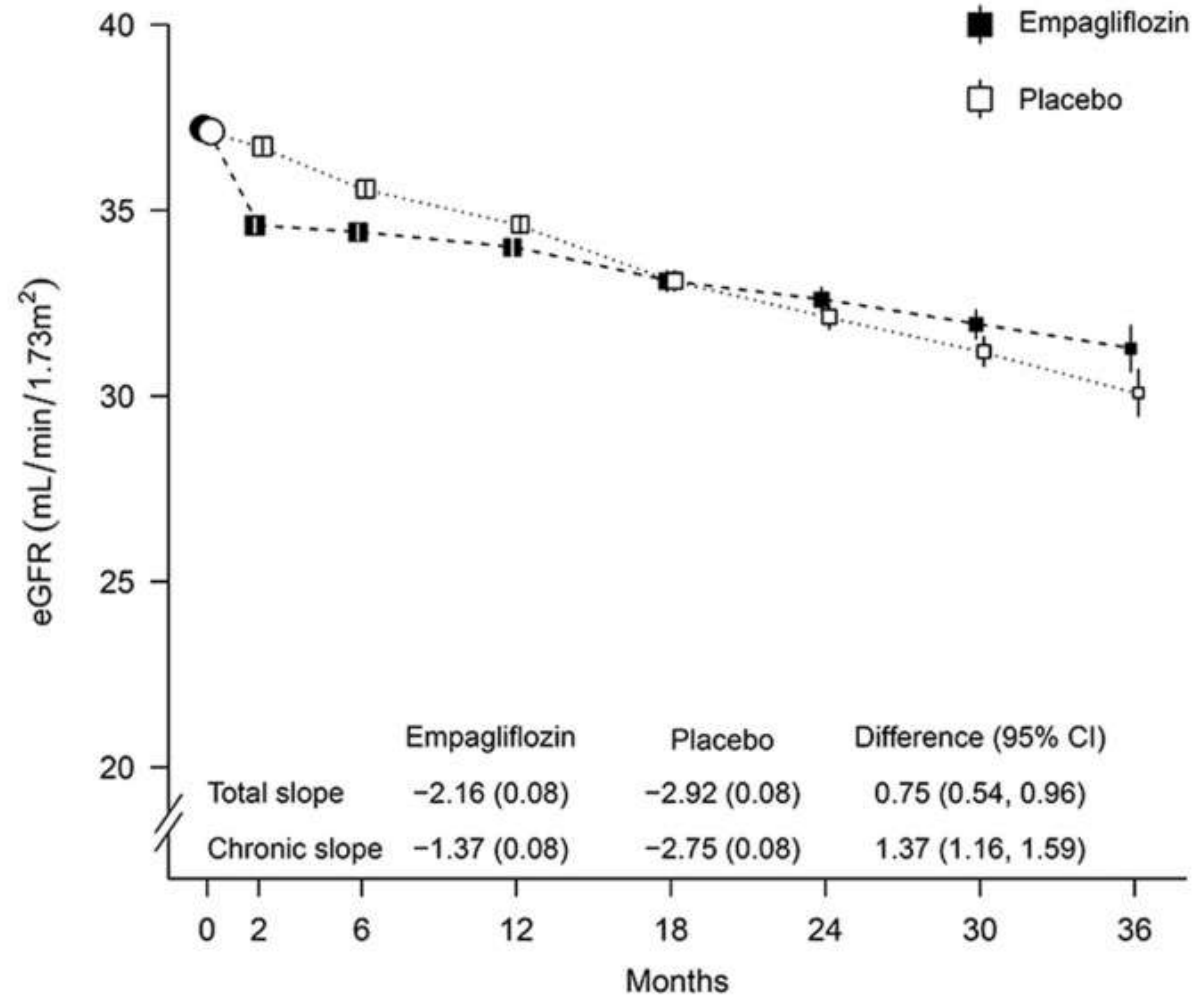
Figure 2.

The primary outcome of kidney disease progression or death from cardiovascular causes occurred in 432 participants (13.1%) in the empagliflozin group and 558 participants (16.9%) in the placebo group. This represented 42 fewer primary outcomes per 1000 patients treated for 2 years.

Empakidney

et al.

Page 14





Conclusioni - IV

- La **fisiopatologia della nefroprotezione** (proteinuria, iperfiltrazione, sovraccarico di volume, chetogenesi, dimagrimento, uricuria, stress tubulare)
- La **selettività per SGLT2/SGLT1**
- Dapagliflozin ed empagliflozin prescrivibili per **GFR** più bassi
- Dapagliflozin non necessita di sospensione per GFR
- Azione antiproteinurica
- Protezione cardiovascolare e renale
- Calo iniziale del GFR

A nighttime cityscape with a bokeh effect of lights, overlaid with a white torn paper effect at the bottom. The text is positioned on the left side of the image.

**GRAZIE PER
L'ATTENZIONE**

Dr M. Golisano

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