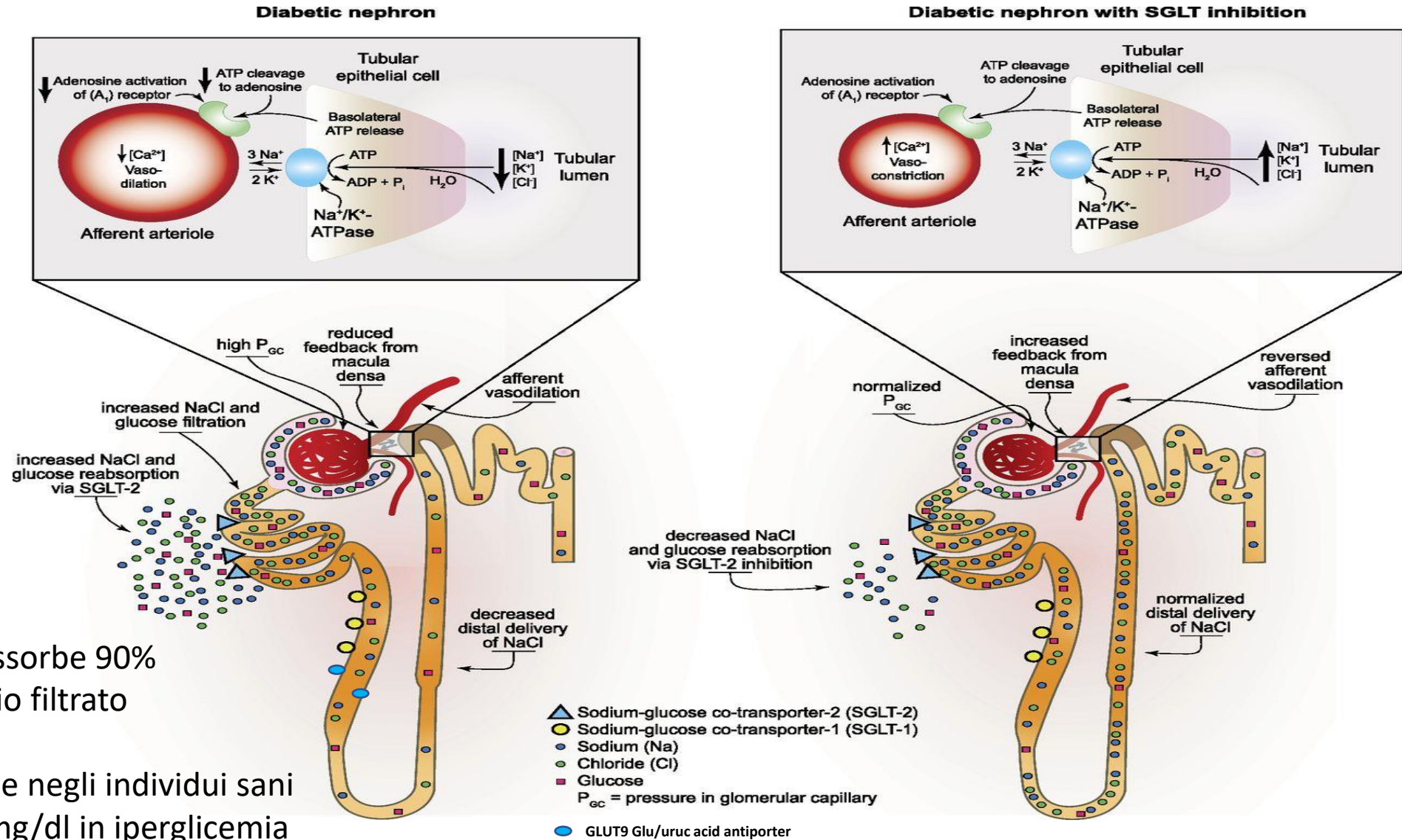


# Sodium/glucose cotransporter 2 (SGLT-2) inhibition and glomerular hemodynamics in diabetes.



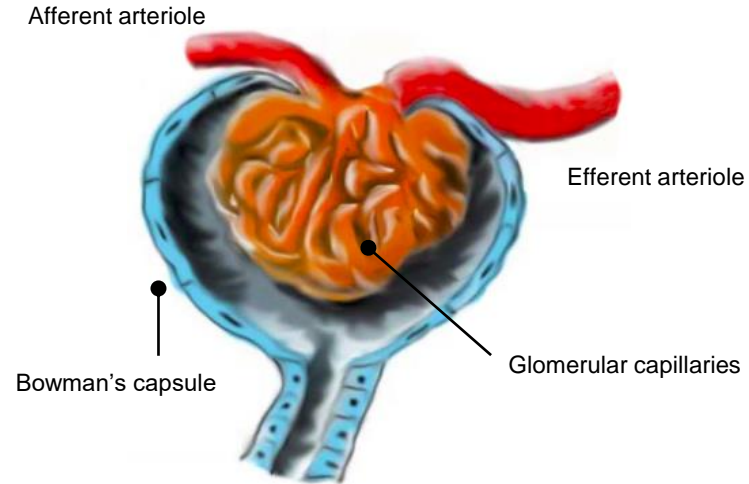
SGLT2 riassorbe 90% del glucosio filtrato

~180 gr/die negli individui sani  
Sino 240 mg/dl in iperglicemia

# SGLT2 inhibition and RAAS inhibition both reduce glomerular pressure and hyperfiltration by complementary mechanisms<sup>1-3</sup>

## RAAS inhibitors

Efferent vasodilation<sup>1</sup>



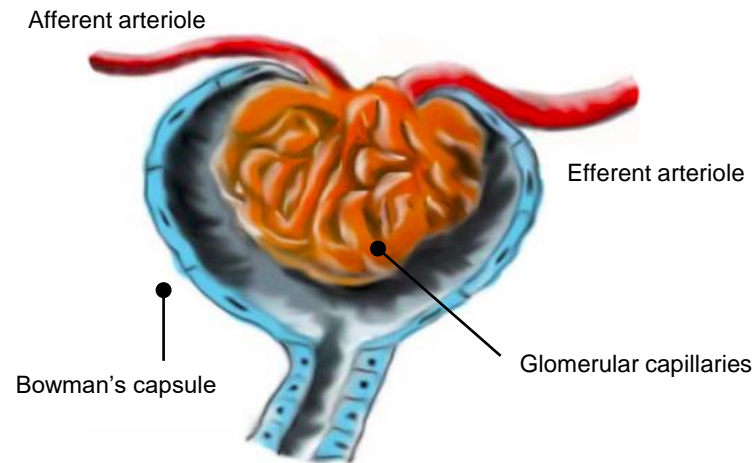
## CLINICAL IMPLICATIONS

- Decreased glomerular pressure<sup>1,3</sup>
- Reduction in albuminuria<sup>1,2</sup>

## SGLT2 inhibitors

Afferent constriction<sup>1-3</sup>

Due to increased Na<sup>+</sup> delivery to the macula densa<sup>1-3</sup>



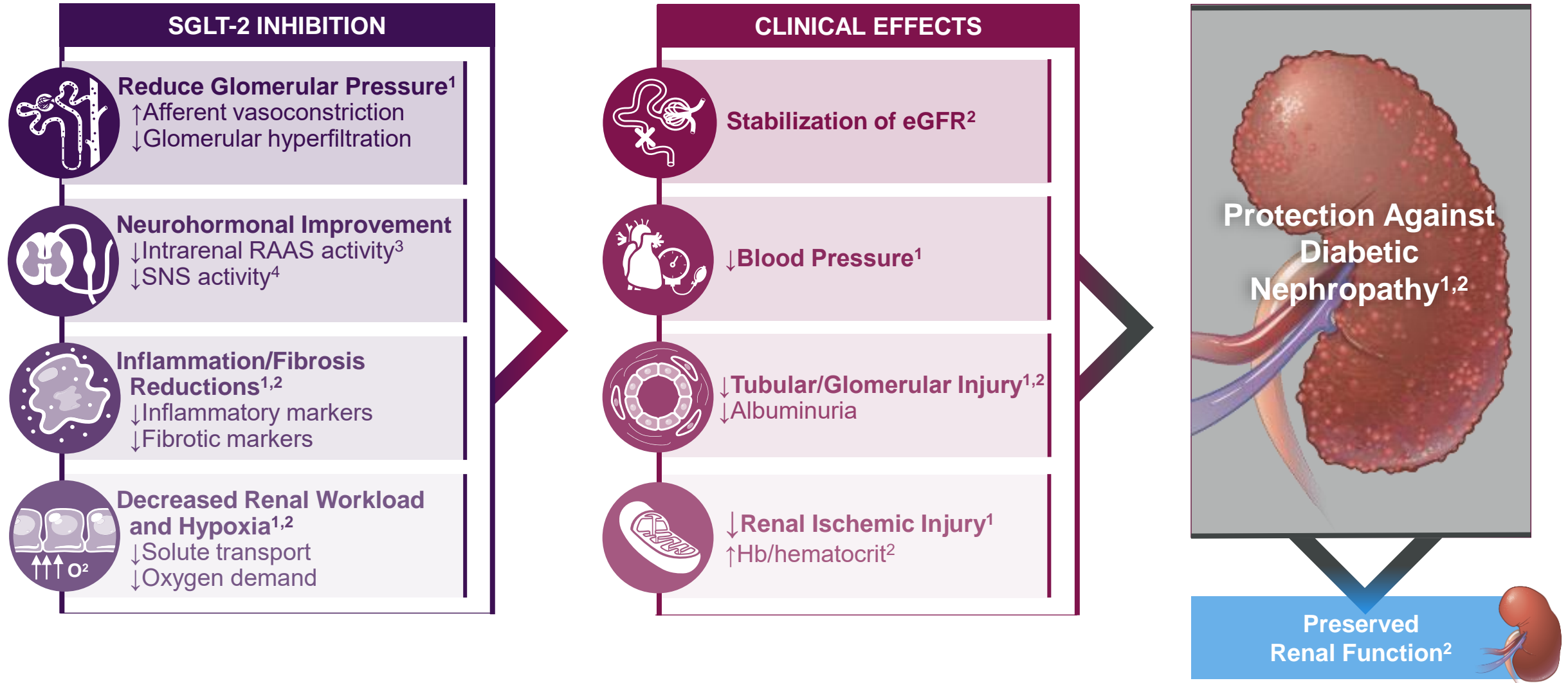
- Decreased glomerular pressure<sup>1,3</sup>
- Reduction in albuminuria<sup>4</sup>

RAAS, renin-angiotensin-aldosterone system; SGLT2, sodium-glucose co-transporter 2

1. Van Bommel EJ, et al. *Clin J Am Soc Nephrol* 2017;12:700-710; 2. Seidu S, et al. *Prim Care Diabetes* 2018;12:265-283; 3. Cherney DZ, et al. *Circulation* 2014;129:587-597;

4. Heerspink HJL, et al. *Diabetes Care* 2011;34(Suppl. 2):S325-S329

# Potential Effects By Which SGLT-2 Inhibition Improves Renal Outcomes



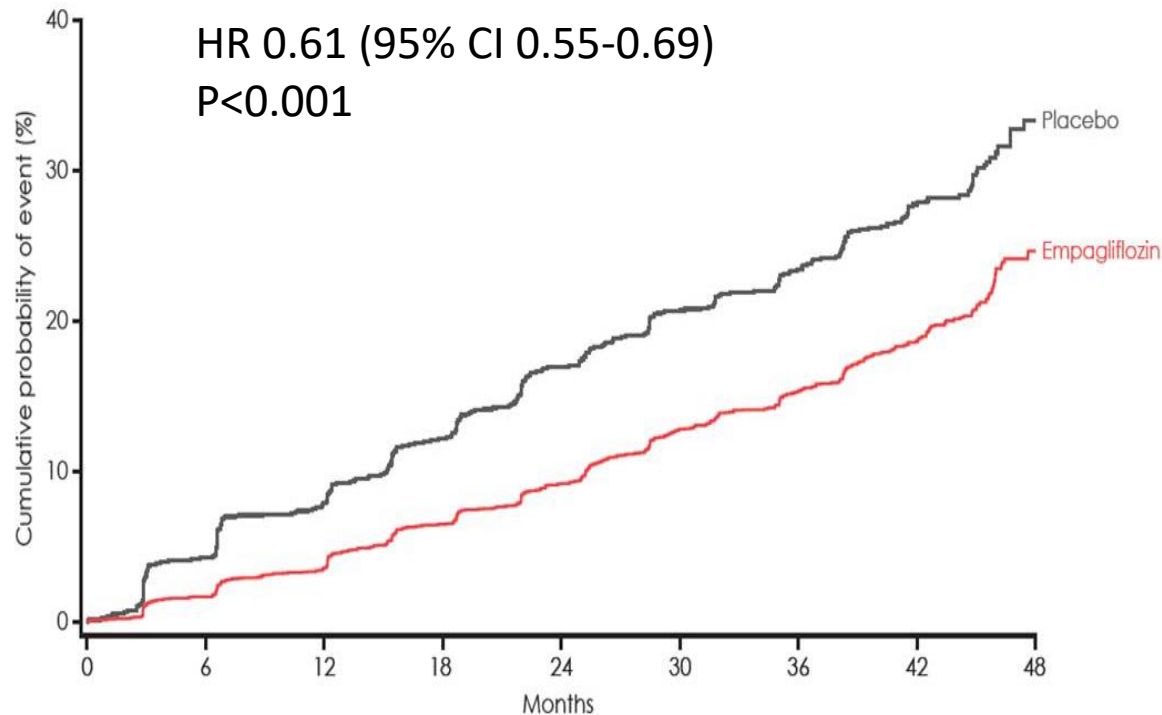
eGFR=estimated glomerular filtration rate; Hb=hemoglobin; RAAS=renin angiotensin aldosterone system; SNS=sympathetic nervous system.

1. Heerspink HJL, et al. *Kidney Int.* 2018;94(1):26-39. 2. Tamargo J. *Eur Cardiol.* 2019;14(1):23-32. 3. Shin SJ, et al. *PLoS One.* 2016;11:e0165703. 4. Sano M. *J Cardiol.*

2018;71(5):471-476.

# Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes

Incidence or worsening of renal dysfunction and CV death

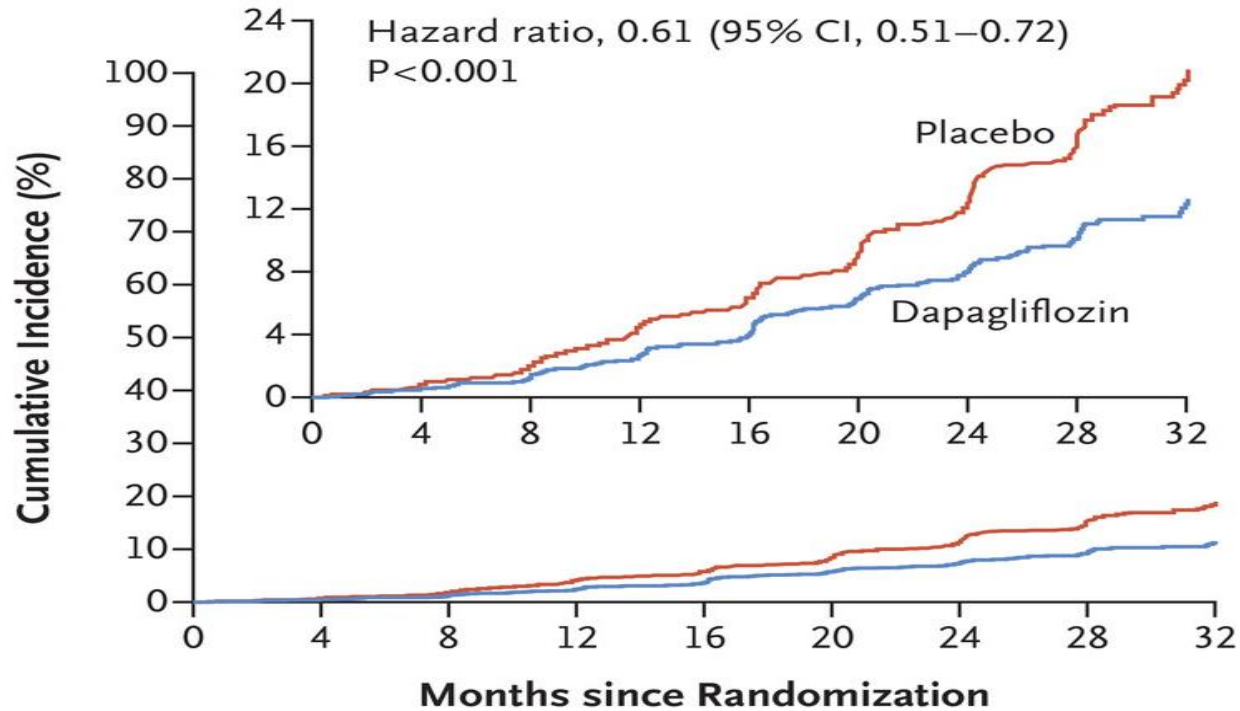


No. of patients	0	6	12	18	24	30	36	42	48
Empagliflozin	4170	4036	3894	3702	3208	2305	1902	1224	291
Placebo	2102	1981	1865	1728	1449	1025	843	526	106

Baseline characteristics	Empagliflozin	Placebo
Type 2 diabetes (%)	100	100
Cardiovascular disease (%)	99	99
Heart failure (%)	10	10
RAASi	81	82
Estimated GFR		
≥60 ml/min/1.73 m <sup>2</sup>	76	75
30 to <60 ml/min/1.73 m <sup>2</sup>	24	25
Urinary albumin-to-creatinine ratio		
< 30	57	59
30-300	28	27
>300	15	14

Incident or worsening nephropathy: progression to macroalbuminuria, doubling of the serum creatinine and eGFR of ≤45 ml/min/1.73 m<sup>2</sup>, initiation of renal-replacement therapy or death from renal disease.

# Dapagliflozin in Patients with Chronic Kidney Disease



No. at Risk	0	4	8	12	16	20	24	28	32
Placebo	2152	1993	1936	1858	1791	1664	1232	774	270
Dapagliflozin	2152	2001	1955	1898	1841	1701	1288	831	309

Primary composite outcome: reduction 50% eGFR; ESRD; renal or CV death

Baseline characteristics	Dapagliflozin	Placebo
Type 2 diabetes (%)	68	67
Cardiovascular disease (%)	38	37
Heart failure (%)	11	11
ACE inhibitor (%)	31	32
ARB (%)	67	66
<b>Estimated GFR</b>		
Mean — ml/min/1.73 m <sup>2</sup>	43±12	43±12
≥60 ml/min/1.73 m <sup>2</sup>	11	10
45 to <60 ml/min/1.73 m <sup>2</sup>	30	32
30 to <45 ml/min/1.73 m <sup>2</sup>	46	43
<30 ml/min/1.73 m <sup>2</sup>	14	15
<b>Urinary albumin-to-creatinine ratio</b>		
Median (interquartile range)	965 (472–1903)	934 (482–1868)
>1000 (%)	49	48

# RACCOMANDAZIONI AMD/SID 2021

## **Pazienti senza precedenti eventi CV**

- 1) Metformina
- 2) GLP1-A o SGLT2i

## **Pazienti con precedenti eventi CV**

- 1) Metformina o GLP1-A o SGLT2i

## **Pazienti con scompenso cardiaco**

- 1) SGLT2-i
- 2) Metformina o SGLT2i

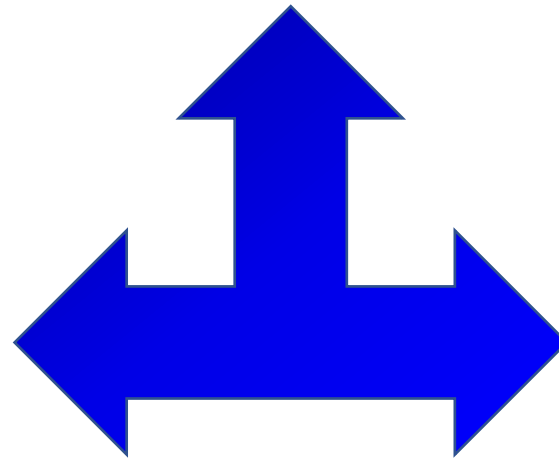
# NORME PRESCRITIVE NOTA 100

Metformina (se GFR >30 ml/min), se tollerata ed efficace  
Se HbA1c > del target individuale (<7% o 52 mmol/mol)

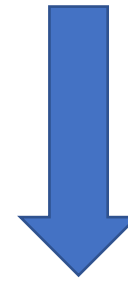
- Prevenzione secondaria
- Rischio CV elevato



SGLT2-i o GLP1-A



- Paziente con MRC  
eGFR 30-60  
e/o A/C >30mg/gr
- Scompenso cardiaco



SGLT2-i

VFG fino a (mL/min*1.73 m <sup>2</sup> )	90	80	70	60	50	40	30	20	15	dialisi
<b>Acarbosio<sup>a</sup></b>										
<b>DPP4i</b>										
Alogliptin										
Linagliptin										
Saxagliptin										
Sitagliptin										
Vildagliptin										
<b>GLP1-RA</b>										
Dulaglutide										
Exenatide										
Exenatide LAR										
Liraglutide										
Lixisenatide										
Semaglutide s.c.										
Semaglutide orale										
<b>Insulina umana/analoghi dell'insulina</b>										
<b>Metformina</b>										
Pioglitazone										
Repaglinide										
<b>SGLT2i</b>										
Canagliflozin <sup>b</sup>										
Dapagliflozin <sup>c</sup>										
Empagliflozin <sup>d</sup>										
Ertugliflozin <sup>d</sup>										
<b>Sulfaniluree</b>										
Glibenclamide										
Gliclazide										
Glimepiride										
Glipizide										
Gliquidone										



**CANA**  
eGFR < 60 → 100 mg  
< 30 non iniziare

**DAPA**  
eGFR < 25 non iniziare

**EMAPA ed ERTU**  
eGFR <45 sospendere