

«WUNDERMITTEL» SGLT-2 INHIBITOREN

**WELCHE PATIENTEN MIT EINER NIERENINSUFFIZIENZ
PROFITIEREN VON EINEM SGLT-2 HEMMER**

**PROF. DR. MED. TOBIAS BREIDTHARDT
FACHARZT FÜR NEPHROLOGIE UND FÜR ALLGEMEINE INNERE MEDIZIN**

«To SGLT2» or «not to SGLT2»

- 55-jähriger Patient, diabetische Nephropathie (eGFR 61ml/min, Proteinurie 3gr/d)
- Langjähriger Diabetes mellitus, inadäquate Therapie. Hba1c 10 %
- St.n. Stroke
- 61 kg bei einer Körpergrösse von 178 cm



Guide to Frequency of Monitoring
(number of times per year) by
GFR and Albuminuria Category

				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased <30 mg/g <3 mg/mmol	Moderately increased 30–300 mg/g 3–30 mg/mmol	Severely increased >300 mg/g >30mg/mmol
GFR categories (ml/min/1.73 m ²) Description and range	G1	Normal or high	≥90	1 if CKD	1	2
	G2	Mildly decreased	60–89	1 if CKD	1	2
	G3a	Mildly to moderately decreased	45–59	1	2	3
	G3b	Moderately to severely decreased	30–44	2	3	3
	G4	Severely decreased	15–29	3	3	4+
	G5	Kidney failure	<15	4+	4+	4+



7000 DM patients
known atherosclerotic disease in 100%
eGFR > 30ml/min

Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes

Renal Outcome Measure	Empagliflozin		Placebo		Hazard Ratio (95% CI)	P Value
	no. with event/ no. analyzed (%)	rate/1000 patient-yr	no. with event/ no. analyzed (%)	rate/1000 patient-yr		
Incident or worsening nephropathy or cardiovascular death	675/4170 (16.2)	60.7	497/2102 (23.6)	95.9	0.61 (0.55–0.69)	<0.001
Incident or worsening nephropathy	525/4124 (12.7)	47.8	388/2061 (18.8)	76.0	0.61 (0.53–0.70)	<0.001
Progression to macroalbuminuria	459/4091 (11.2)	41.8	330/2033 (16.2)	64.9	0.62 (0.54–0.72)	<0.001
Doubling of serum creatinine level accompanied by eGFR of ≤ 45 ml/min/1.73 m ²	70/4645 (1.5)	5.5	60/2323 (2.6)	9.7	0.56 (0.39–0.79)	<0.001
Initiation of renal-replacement therapy	13/4687 (0.3)	1.0	14/2333 (0.6)	2.1	0.45 (0.21–0.97)	0.04
Doubling of serum creatinine level accompanied by eGFR of ≤ 45 ml/min/1.73 m ² , initiation of renal-replacement therapy, or death from renal disease	81/4645 (1.7)	6.3	71/2323 (3.1)	11.5	0.54 (0.40–0.75)	<0.001
Incident albuminuria in patients with a normal albumin level at baseline	1430/2779 (51.5)	252.5	703/1374 (51.2)	266.0	0.95 (0.87–1.04)	0.25

0.125 0.25 0.5 1.0 2.0 4.0

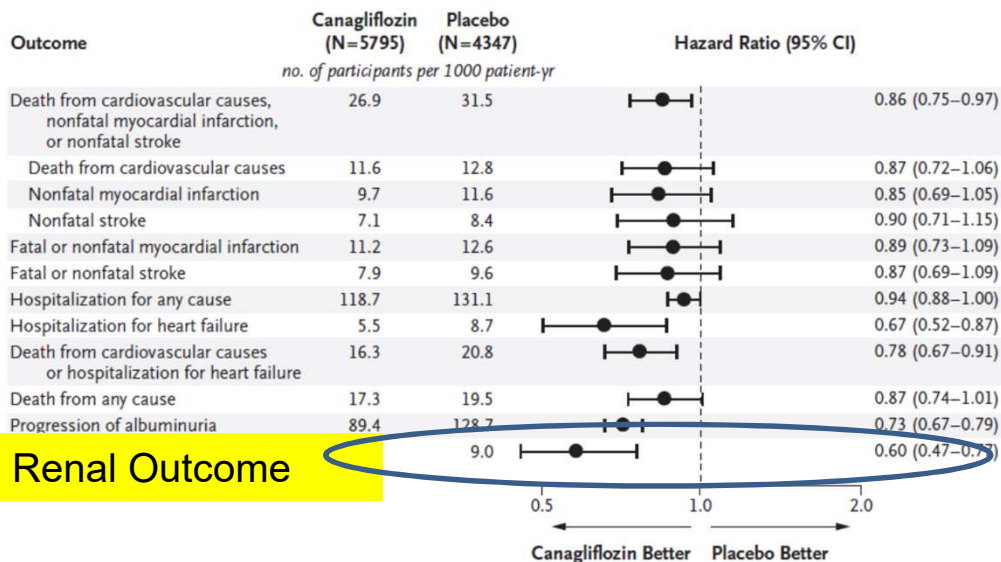
← Empagliflozin better | Placebo better →

ORIGINAL ARTICLE

2017

Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes

10000 DM patients
known atherosclerotic disease in 72%
eGFR > 30ml/min

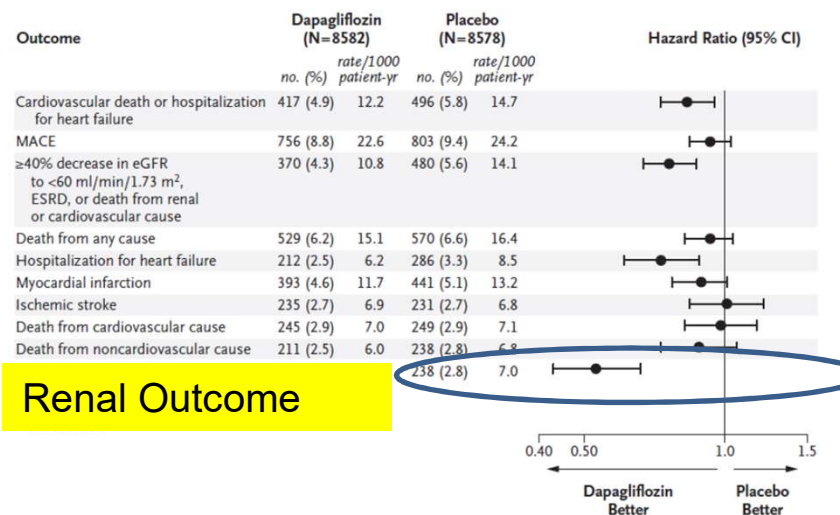


ORIGINAL ARTICLE

2019

Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes

17000 DM patients
known atherosclerotic disease in 40%
eGFR > 60ml/min

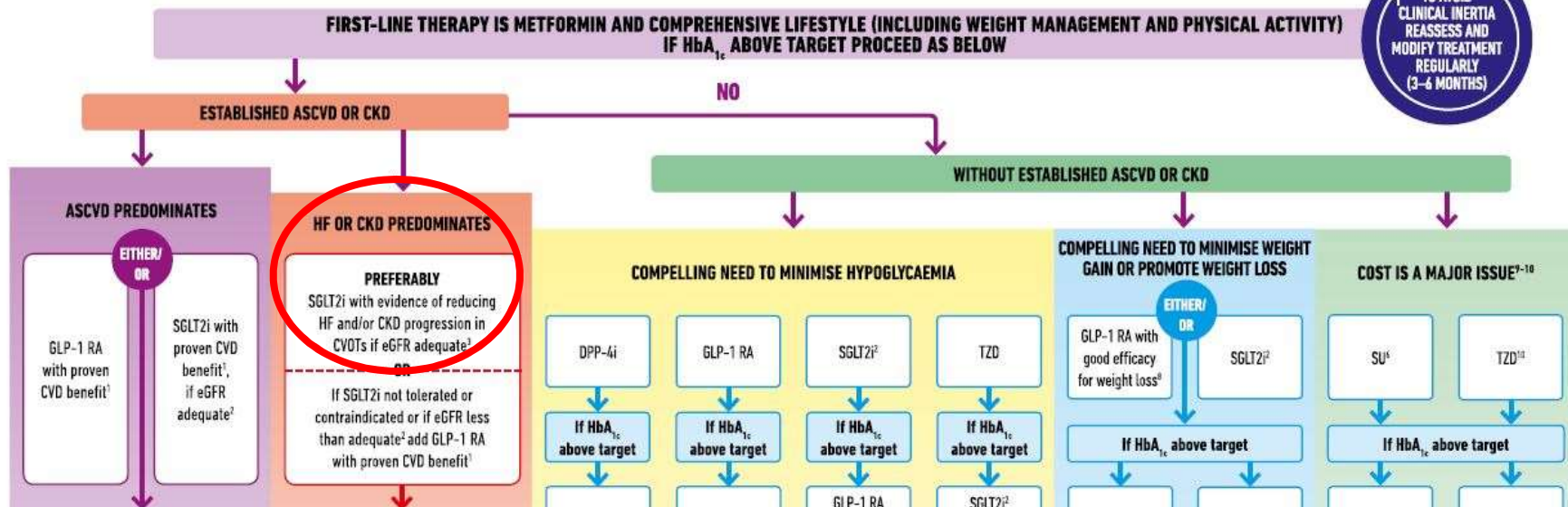


2022 EASD/ADA Diabetes Type 2 Guidelines



GLUCOSE-LOWERING MEDICATION IN TYPE 2 DIABETES: OVERALL APPROACH

TO AVOID CLINICAL INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3-6 MONTHS)



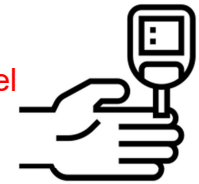
We recommend treating patients with T2D, CKD, and an eGFR \geq 30 ml/min per 1.73 m² with an SGLT2i

To «SGLT2» or «not to SGLT2»

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0.2 % euglykämie Ketoacidose
-Risiko: schlanker Typ 2
Langjähriger DM; Insulinmangel

+ Insulin



To «SGLT2» or «not to SGLT2»

- 55-jähriger Patient, eGFR 70ml/min,
- Langjähriger Diabetes mellitus, inadäquat eingestellt
- Arterielle Hypertonie, St.n. Stroke
- 61 kg bei einer Körpergröße von 175 cm

- 45-jährige Patientin
- CKD bei sekundärer fokal-segmentärer Glomerulosklerose
- Ramipril 10mg/d

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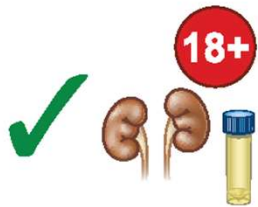
RCT Protocol

Dapagliflozin and prevention of adverse outcomes in chronic kidney disease (DAPA-CKD)

Rationale and trial protocol

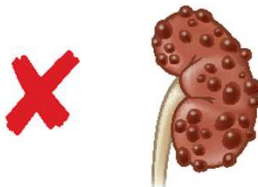


Multicentre ~ 400
Target n = 4300
Patients with and without type 2 diabetes



18+

≥ 18 years
25–75 ml/min/1.73 m²
uACR ≥ 200 mg/g



4300 HF patients
eGFR mean: 42ml/min
< 30ml/min: 14%

Mean proteinuria: 900mg/d

Interventions



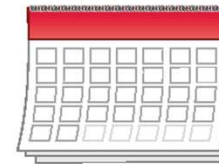
Dapagliflozin
10 mg

1:1



Placebo

Follow-up



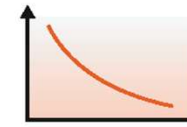
~ 45 months



Event-driven
(681 events)

Primary outcome

Composite renal endpoint



≥ 50% decline
in eGFR



End-stage
kidney disease



Renal or
cardiovascular
death

Dapagliflozin in Patients with Chronic Kidney Disease

Table 2. Primary and Secondary Outcomes and Adverse Events of Special Interest.*

Outcome	Dapagliflozin		Placebo		Hazard Ratio (95% CI)	P Value
	no./total no. (%)	events/100 patient-yr	no./total no. (%)	events/100 patient-yr		
NNT 19 [95% CI, 15 to 27] Blister mit 98 Tbl CHF 201.95.-						
Primary outcome						
Primary composite outcome	197/2152 (9.2)	4.6	312/2152 (14.5)	7.5	0.61 (0.51–0.72)	<0.001
Decline in estimated GFR of $\geq 50\%$	112/2152 (5.2)	2.6	201/2152 (9.3)	4.8	0.53 (0.42–0.67)	NA
End-stage kidney disease	109/2152 (5.1)	2.5	161/2152 (7.5)	3.8	0.64 (0.50–0.82)	NA
Estimated GFR of <15 ml/min/1.73 m ²	84/2152 (3.9)	1.9	120/2152 (5.6)	2.8	0.67 (0.51–0.88)	NA
Long-term dialysis [†]	68/2152 (3.2)	1.5	99/2152 (4.6)	2.2	0.66 (0.48–0.90)	NA
Kidney transplantation [†]	3/2152 (0.1)	0.1	8/2152 (0.4)	0.2	—	NA
Death from renal causes	2/2152 (<0.1)	0.0	6/2152 (0.3)	0.1	—	NA
Death from cardiovascular causes	65/2152 (3.0)	1.4	80/2152 (3.7)	1.7	0.81 (0.58–1.12)	NA
Secondary outcomes						
Composite of decline in estimated GFR of $\geq 50\%$, end-stage kidney disease, or death from renal causes	142/2152 (6.6)	3.3	243/2152 (11.3)	5.8	0.56 (0.45–0.68)	<0.001
Composite of death from cardiovascular causes or hospitalization for heart failure	100/2152 (4.6)	2.2	138/2152 (6.4)	3.0	0.71 (0.55–0.92)	0.009
Death from any cause	101/2152 (4.7)	2.2	146/2152 (6.8)	3.1	0.69 (0.53–0.88)	0.004



Dapa CKD

compendium.ch®

09.08.21:

Zulassung für die Senkung
des Risikos der Progression
einer CKD

Cave: Limitatio und BAG-
Reimbursement ausstehend

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- 55-jähriger Patient, eGFR 70ml/min, Proteinurie 3gr/d
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+ Insulin



- 45-jährige Patientin
- CKD bei sekundärer fokal-segmentaler Glomerulosklerose (eGFR 35/min/min, Proteinurie ca 1/2gr)
- Ramipril 10mg/d



What to expect when you «SGLT2»

Urine Glucose

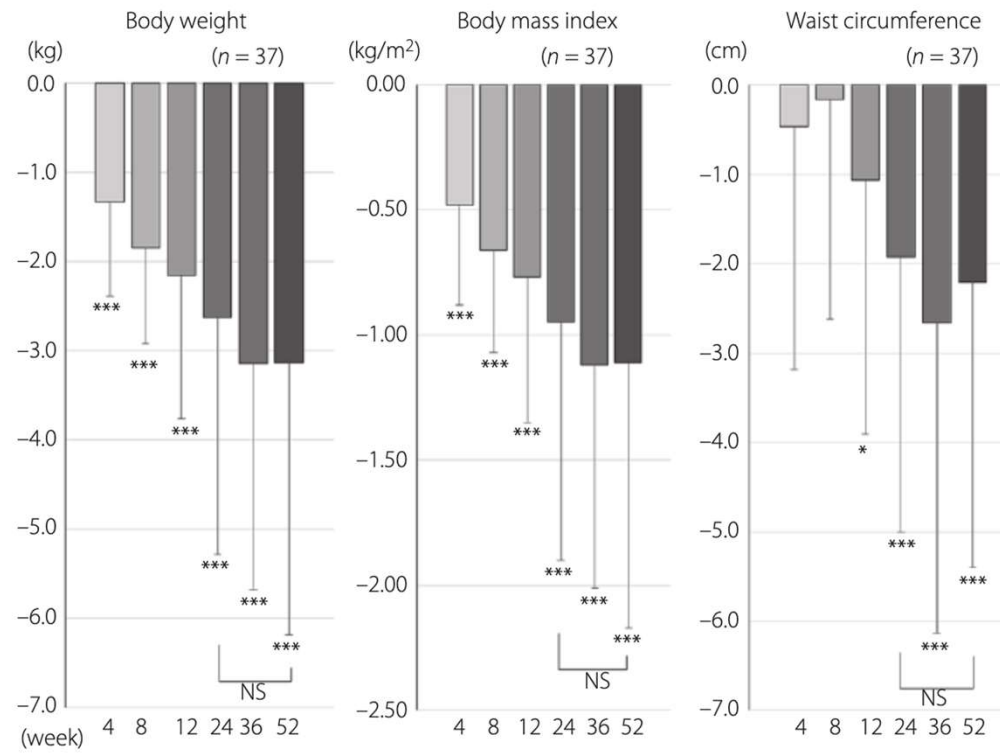
Wert
+++
++
angef.
+++
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+++
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negativ
negativ
negativ

Glukosurie / Tag mit SGLT2i

**50-80 g Glucose =
200-320 Kalorien =
12 – 20 Zuckerwürfeln**



What to expect when you «SGLT2»



What to expect when you «SGLT2»

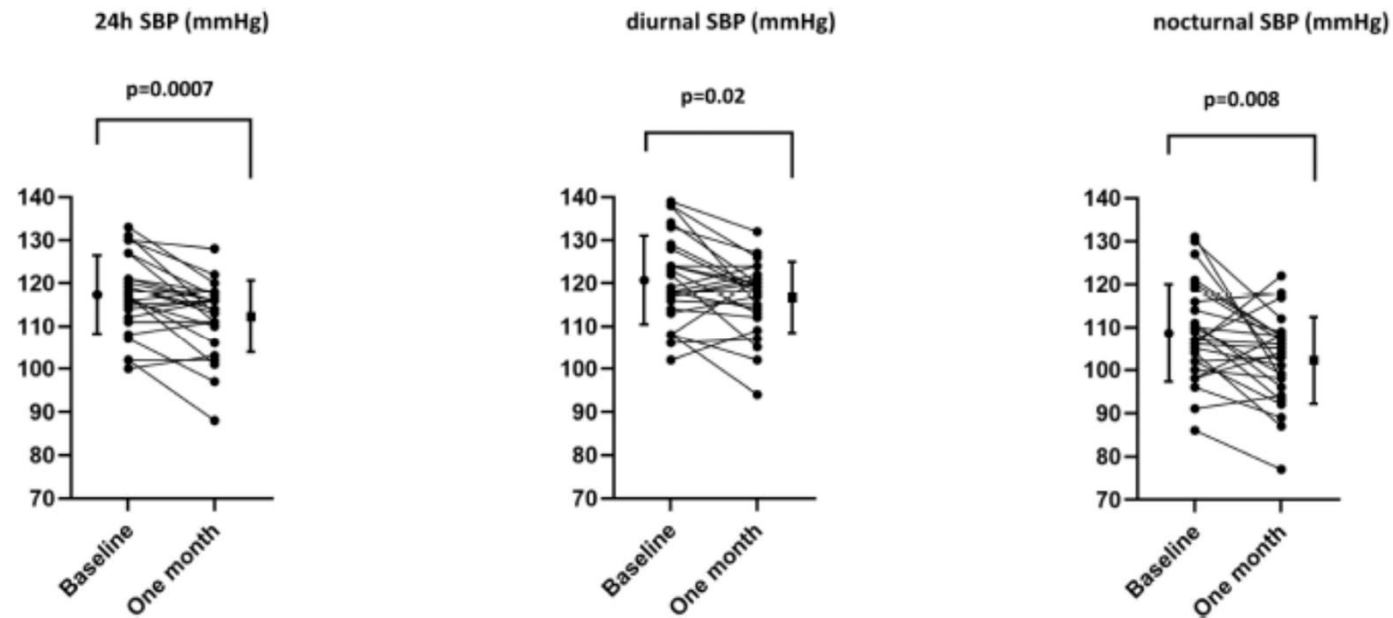


FIGURE 2 | Individual variations in 24 h, diurnal, and nocturnal systolic blood pressure with empagliflozin.

What to expect when you «SGLT2»

Urine Glucose

Wert
+++
++
angef.
+++
+++
+++
++
negativ
negativ
negativ

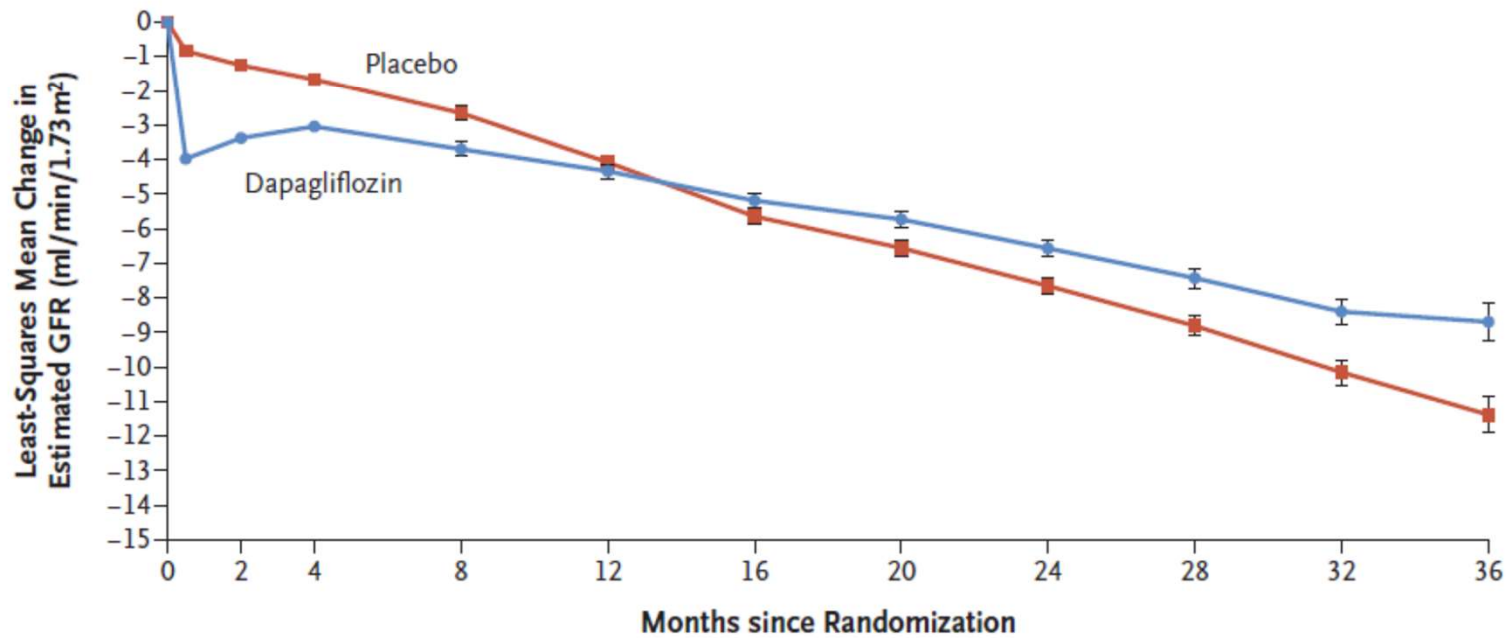
Urine Protein

Wert	Einheit
nbr	mg/mmol
nicht berechenbar	
17.9 +	mg/mmol
15.4 +	mg/mmol
14.3 +	mg/mmol
25.0 +	mg/mmol
55.2 +	mg/mmol

Serum Creatinine

Wert
199 +
206 +
angef.
195 +
172 +
185 +
178 +
164 +
161 +

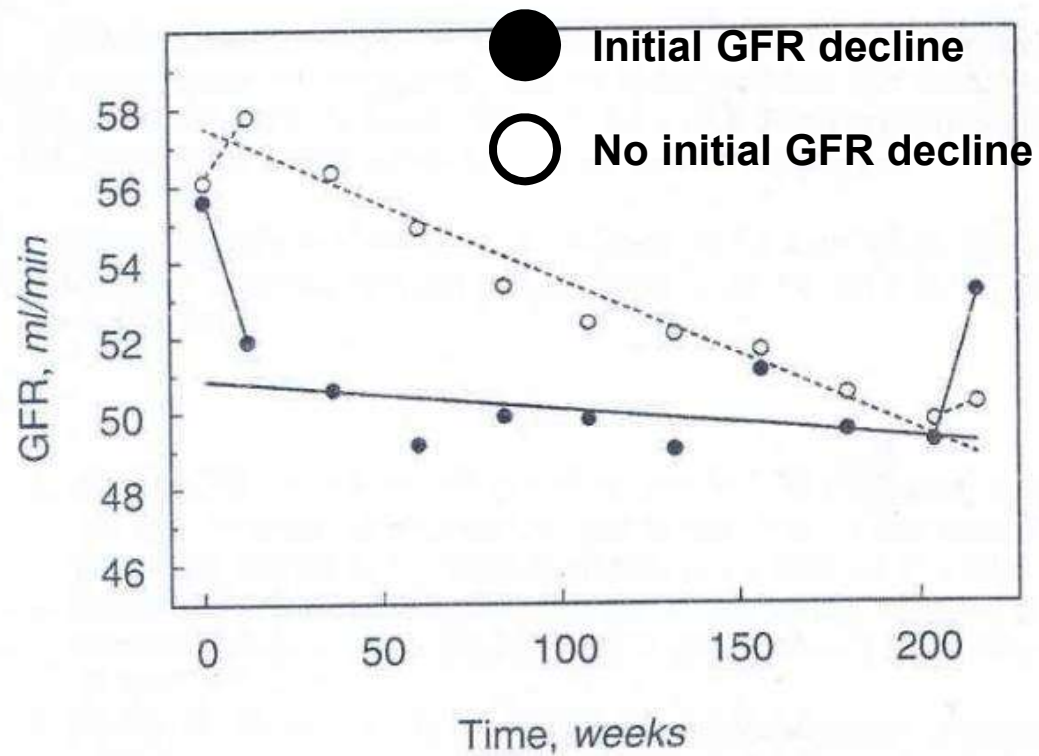
Dapagliflozin in Patients with Chronic Kidney Disease

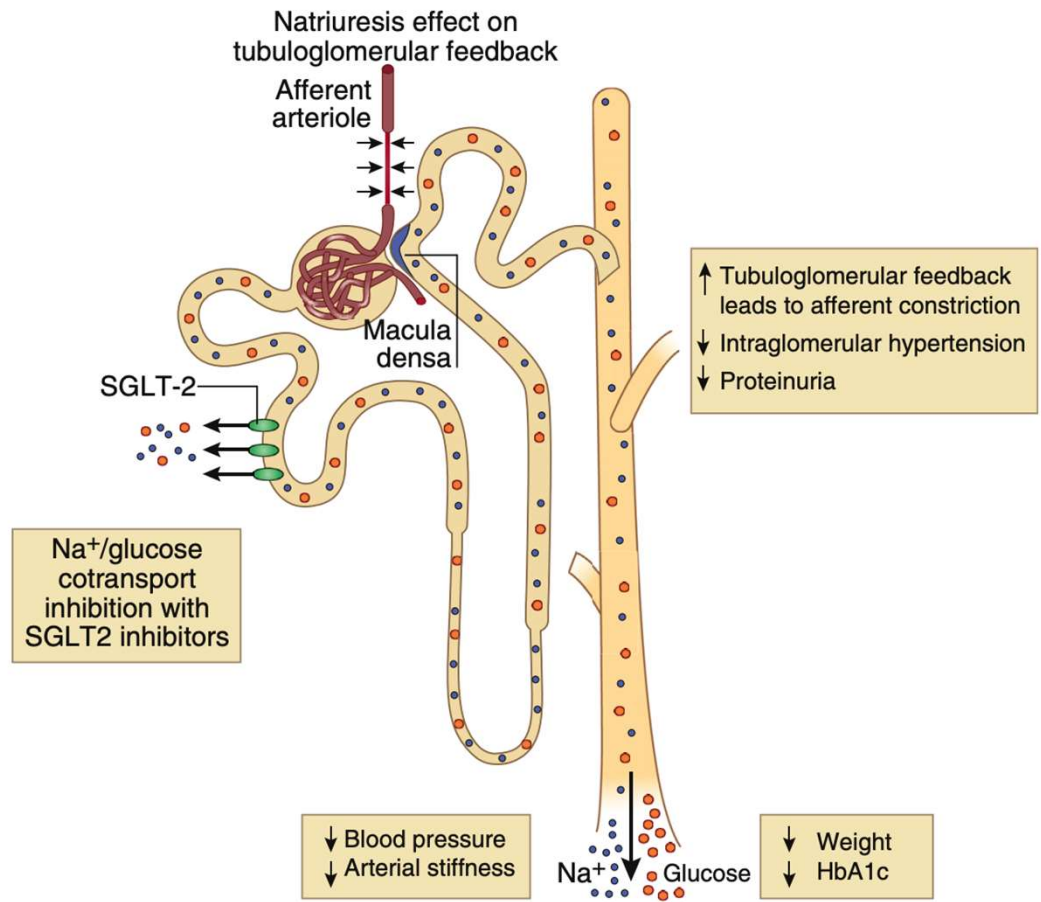


No. of Participants

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

Renal Hemodynamics





Wo stehen wir

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Diabetes mellitus IA
(CKD 30%)

-Empa-Reg; Canvas; Declare

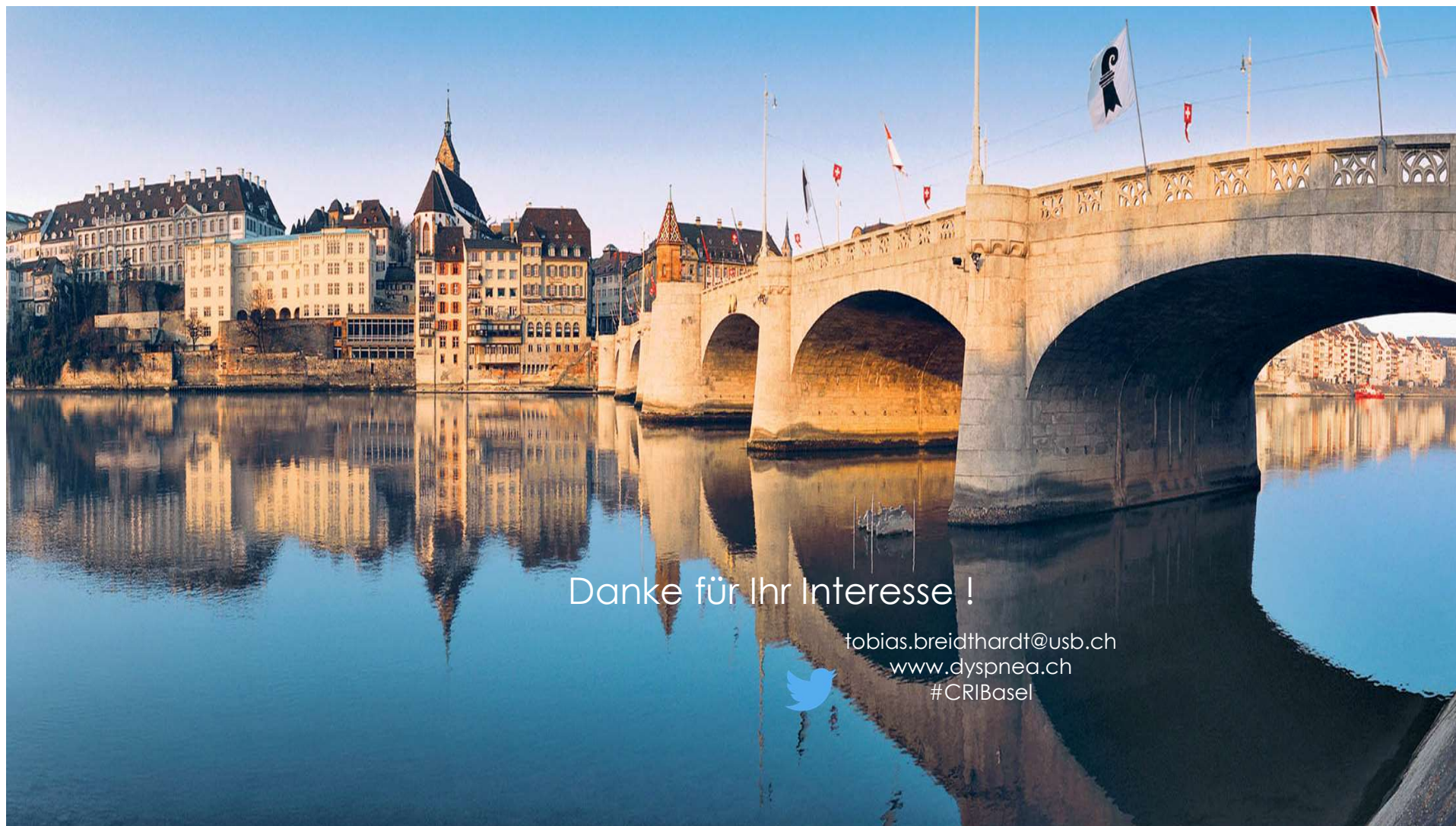
HFrEF IA
(CKD 40-50%)

-Emperor reduced; Dapa HF

Proteinuric CKD

- Dapa CKD

Empa Kidney



Danke für Ihr Interesse !

tobias.breidhardt@usb.ch
www.dyspnea.ch
#CRIBasel

