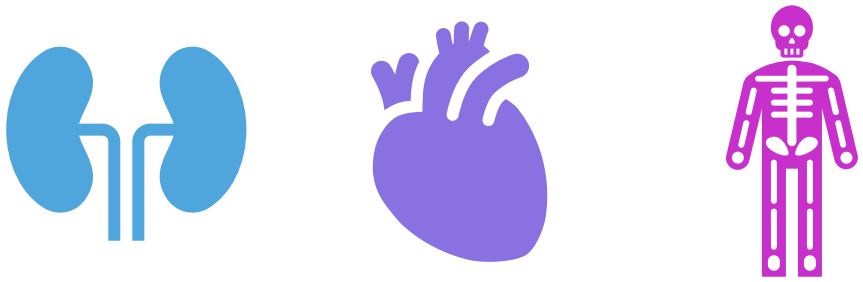
SGLT2 Inhibitors in Heart Failure Management:

Risk Reduction or Risking it all?



Dominique Monteleone, PharmD

January 14, 2020

Abbreviations

- ACEi: angiotensin-converting enzyme inhibitor
- ADHF: acute decompensated heart failure
- AKI: acute kidney injury
- ARB: angiotensin-receptor blocker
- CKD: chronic kidney disease
- COPD: chronic obstructive pulmonary disease
- CV: cardiovascular
- DKA: diabetic ketoacidosis
- DM2: type 2 diabetes
- ESKD: end-stage kidney disease
- ESRD: end-stage renal disease
- GDMT: guideline-directed medical therapy
- GU: genitourinary
- HF: heart failure
- HFrEF: heart failure with reduced ejection fraction
- HFpEF: heart failure with preserved ejection fraction
- MACE: major adverse cardiovascular event
- NT-proBNP: N-terminal prohormone B-type natriuretic peptide
- RAAS: renin-angiotensin-aldosterone system
- SGLT2: sodium-glucose cotransporter 2

Objectives

- Review the literature of SGLT2 inhibitor efficacy in heart failure
- Evaluate the safety of SGLT2 inhibitors in patients with heart failure
- Discuss the monitoring and management of SGLT2 inhibitors in heart failure patients

Heart Failure Mortality Statistics

- Mortality rate at 1-year post heart failure (HF) hospitalization discharge: 20%
- Readmission rate after HF hospitalization: 50%
- 5-year mortality rate (HF with reduced ejection fraction): 50%
- Mortality risk increases 25% in patients with both HF and chronic kidney disease

Shah KS et al. J Am Coll Cardiol. 2017;70:2476–2486.
Heart Disease and Stroke Statistics 2017 update. Circulation. 2017 March 07; 135(10): e146–e603. doi:10.1161/CIR.0000000000000485

Unmet Needs in HF Management

HFrEF

- Proportion of patients on guideline-recommended **doses** of:
  - ACE inhibitors: 22%
  - Beta blockers : 12%

HFpEF

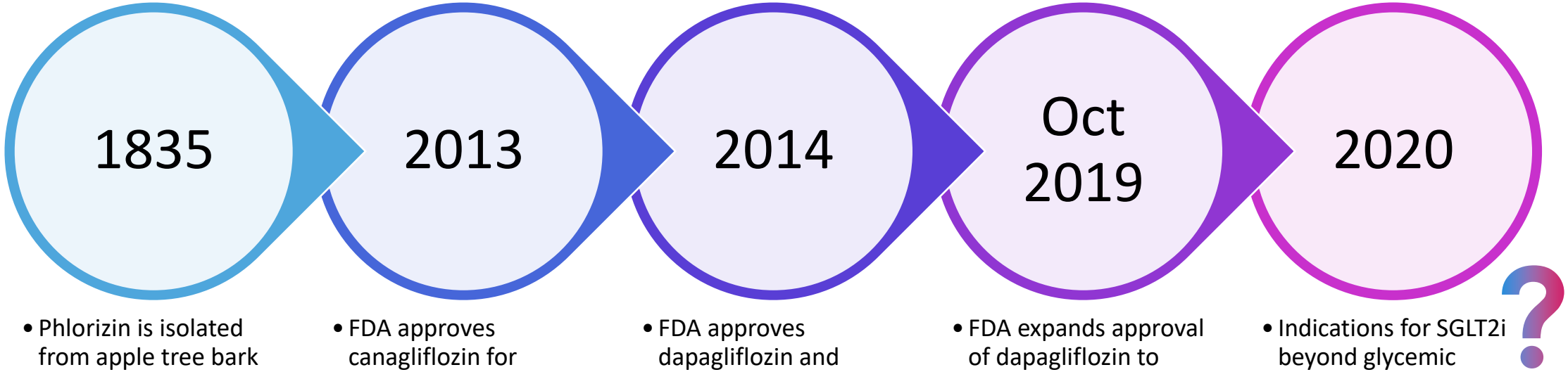
- No therapies with proven mortality benefit

Cardiorenal syndrome

- Current treatment options are inadequate

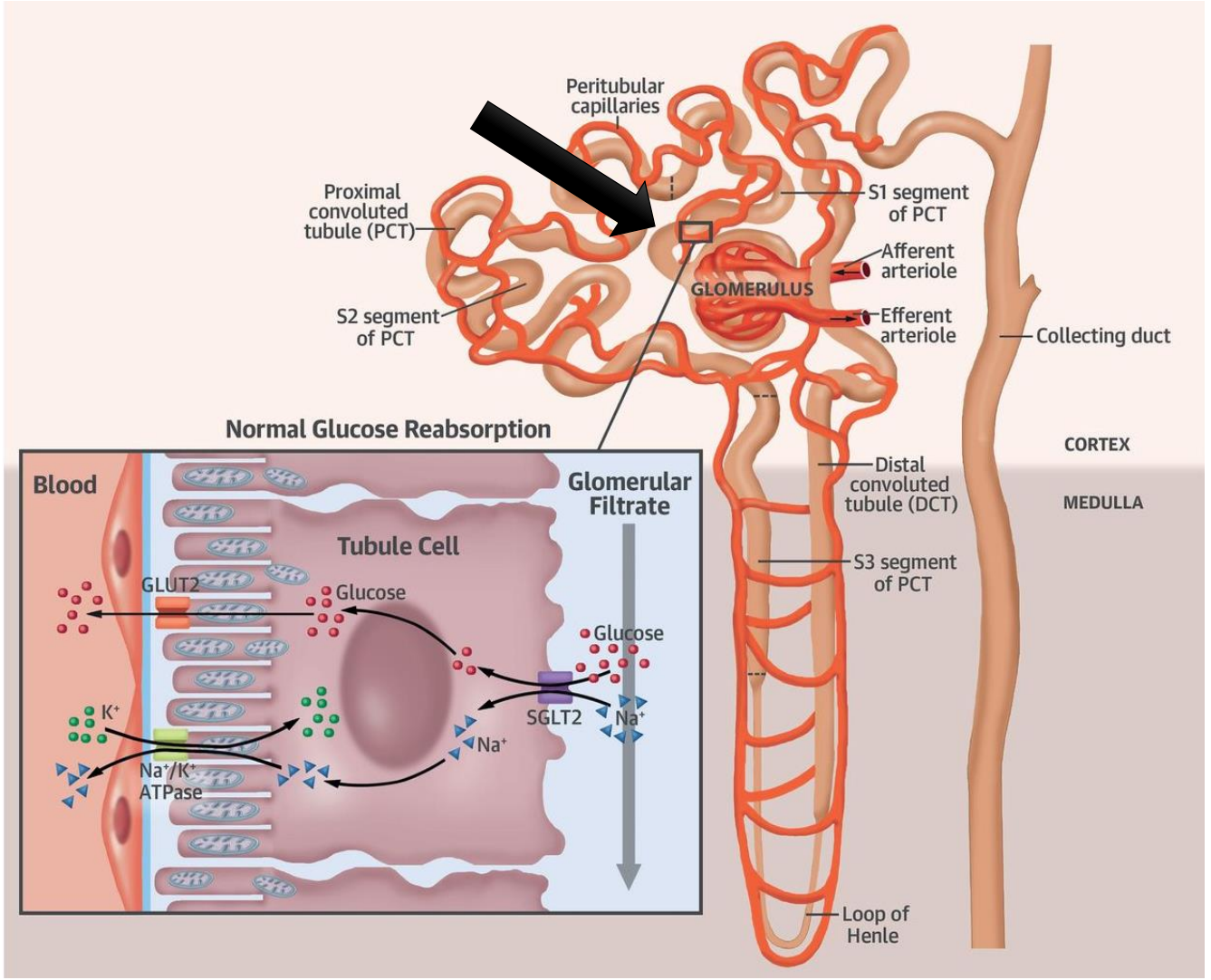
Ouwerkerk W ett al. Eur Heart J. 2017;38:1883–1890.
Lam CS, et al. J Am Heart Assoc. 2019;8:e013389.

The History & Future of SGLT2 Inhibitors

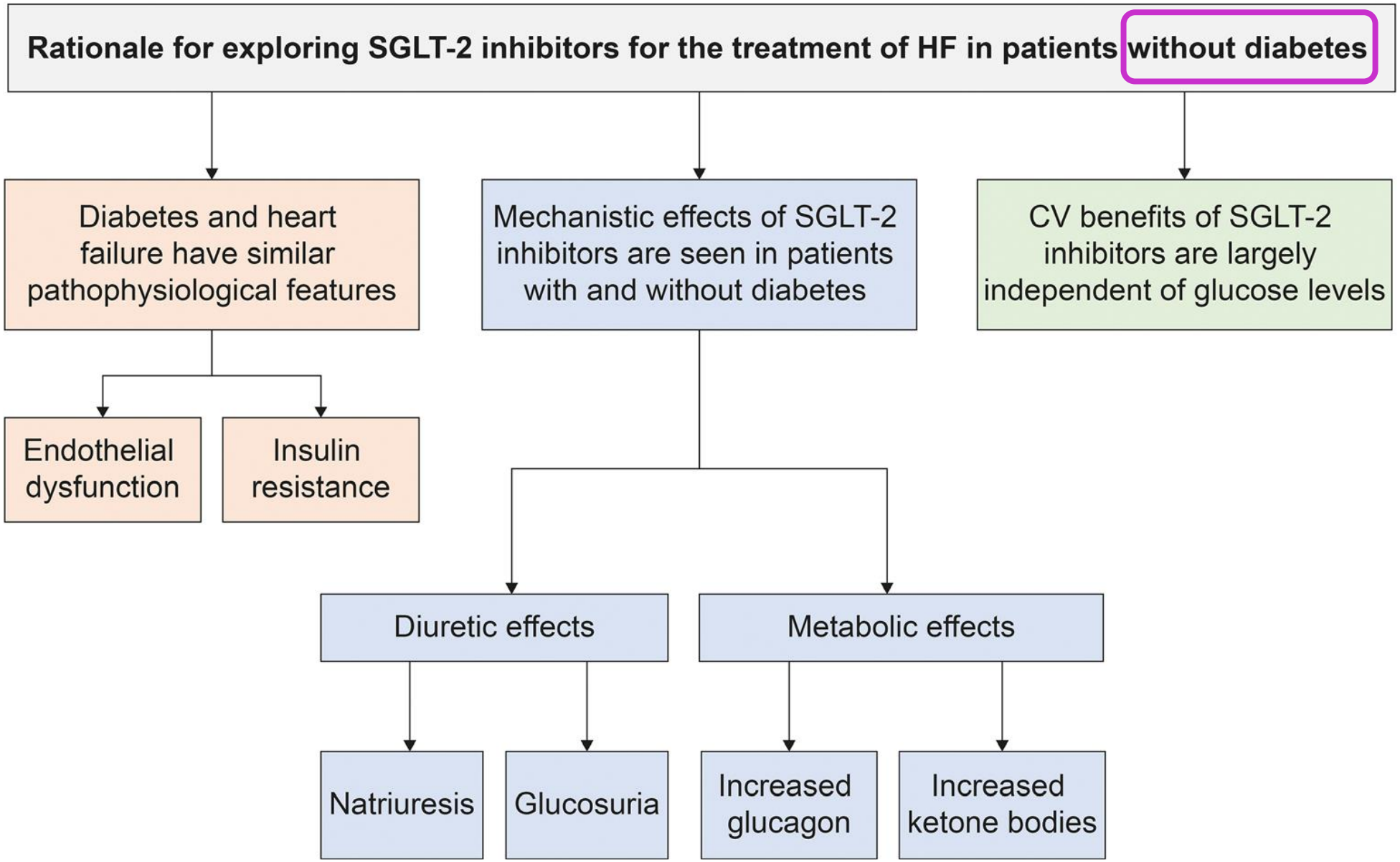


Zelniker TA et al. J Am Coll Cardiol. 2018;72(15):1845-55.

SGLT2 Inhibitor Mechanism of Action



Zelniker TA et al. J Am Coll Cardiol. 2018;72(15):1845-55.



Lam CS et al. J Am Heart Assoc. 2019;8:e013389.

Good News or Causing Controversy?

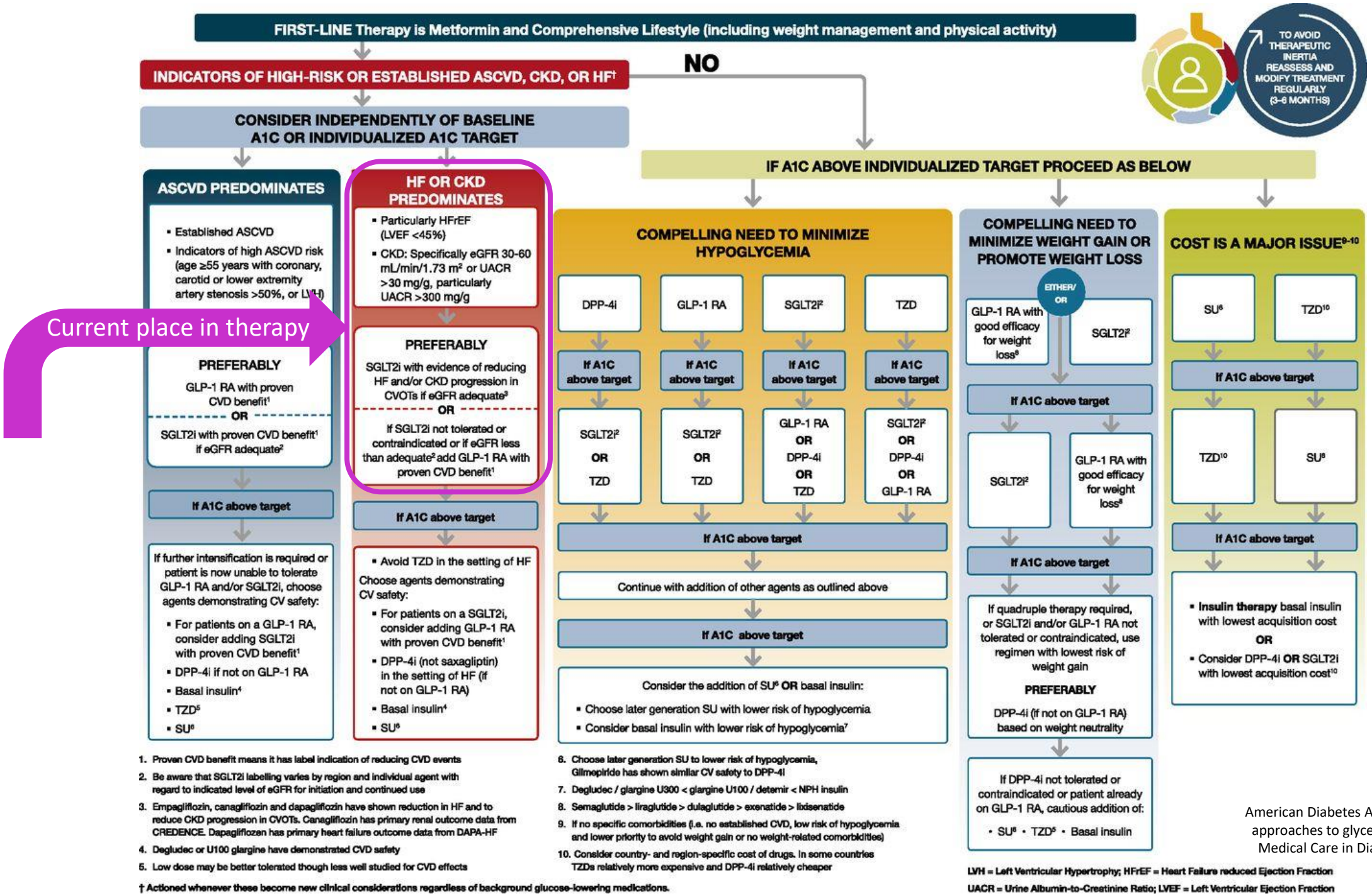
- SGLT2 inhibitors have warnings for use in patients with diabetes
- SGLT2 inhibitors may soon be used for patients with heart failure (with or without diabetes) who are on other medications that affect renal function and volume status

Key Question:
Are SGLT2 inhibitors safe in heart failure patients?

Cardiovascular Outcome Trials

Trial	EMPA-REG OUTCOME[1]	CANVAS[2]	DECLARE-TIMI 58[3]
Sample size	n=7,020	n=10,142	n=17,160
History of HF	10%	14.4%	10%
Methods	Empagliflozin 10 mg or 25 mg daily vs. placebo	Canagliflozin 100 mg or 300 mg daily vs. placebo	Dapagliflozin 10 mg daily vs. placebo
Results [HR (95% CI)]			
MACE	0.86 (0.74-0.99)	0.86 (0.75-0.97)	0.93 (0.84-1.03)
CV mortality	0.62 (0.49-0.77)	0.87 (0.72-1.06)	0.98 (0.82-1.17)
Total mortality	0.68 (0.57-0.82)	0.87 (0.74-1.01)	0.93 (0.82-1.04)
Hospitalization for HF	0.65 (0.50-0.85)	0.67 (0.52-0.87)	0.73 (0.6-0.88)

1. Zinman B et al. N Engl J Med 2015;373:2117-28.
2. Neal B et al. N Engl J Med 2017;377:644-57.
3. Wiviott SD et al. N Engl J Med 2019;380:347-57.



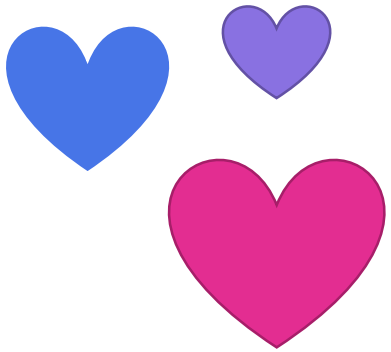
1. Proven CVD benefit means it has label indication of reducing CVD events
2. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Empagliflozin, canagliflozin and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin has primary renal outcome data from CREDENCE. Dapagliflozen has primary heart failure outcome data from DAPA-HF
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU to lower risk of hypoglycemia, Glimepiride has shown similar CV safety to DPP-4i
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e. no established CVD, low risk of hypoglycemia and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

LVH = Left Ventricular Hypertrophy; HFrEF = Heart Failure reduced Ejection Fraction
UACR = Urine Albumin-to-Creatinine Ratio; LVEF = Left Ventricular Ejection Fraction

American Diabetes Association. 2. Pharmacologic approaches to glycemic treatment: Standards of Medical Care in Diabetes—2020. Diabetes Care 2020;43(Suppl. 1):S98–S110.

DAPA-HF



Dapagliflozin in patients with heart failure and reduced ejection fraction (DAPA-HF)	
Study Design	Randomized, placebo-controlled, phase 3 trial
Objective	To evaluate the efficacy and safety of dapagliflozin in patients with heart failure and a reduced ejection fraction, **regardless of the presence or absence of diabetes**
Methods	Dapagliflozin 10 mg once daily or placebo
Key Inclusion Criteria	Age ≥ 18 years Symptomatic HFrEF (LVEF ≤ 40% and NYHA functional class II-IV) Elevated NT-proBNP Standard heart failure therapy
Key Exclusion Criteria	Type 1 diabetes mellitus Symptoms of hypotension or SBP <95 mmHg eGFR<30 mL/min/1.73m^2 Hospitalization due to decompensated HF within 4 weeks prior to enrollment
Primary Endpoint	Composite of worsening heart failure (hospitalization or urgent visit requiring IV therapy for heart failure) or cardiovascular death

McMurray JJV et al. N Engl J Med 2019;381:1995-2008.

DAPA-HF Baseline Characteristics

Baseline Characteristics		
Characteristic – no, %	**Dapagliflozin (n=2373)**	**Placebo (n=2371)**
Age, years	66.2±11.0	66.5±10.8
Female	564 (23.8)	545 (23.0)
NYHA Classification		
II	1606 (67.7)	1597 (67.4)
III	747 (31.5)	751 (31.7)
LVEF, %	31.2±6.7	30.9±6.9
History of HF hospitalization	1124 (47.4)	1127 (47.5)
Diabetes	993 (41.8)	990 (41.8)
Mean eGFR	66.0±19.6	65.5±19.3
HF Medications		
ACE inhibitor	1332 (56.1)	1329 (56.1)
ARB	675 (28.4)	632 (26.7)
Sacubitril-valsartan	250 (10.5)	258 (10.9)
Beta-blocker	2278 (96.0)	2280 (96.2)
MRA	1696 (71.5)	1674 (70.6)
Diuretic	2216 (93.4)	2217 (93.5)

McMurray JJV et al. Eur J Heart Fail 2019;21:1402-1411.

DAPA-HF Results

NNT 21

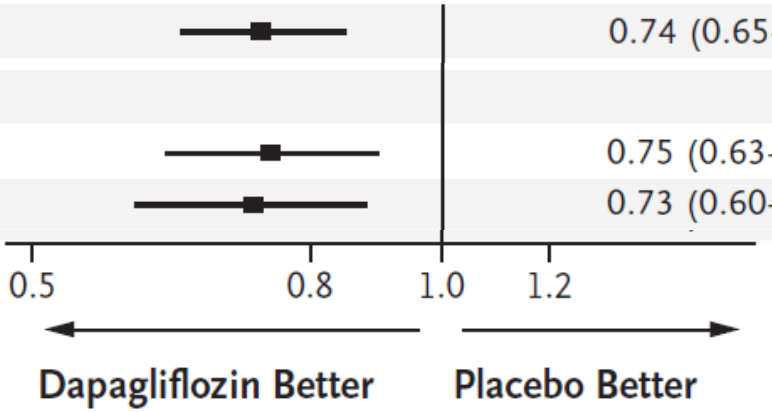
Table 2. Primary and Secondary Cardiovascular Outcomes and Adverse Events of Special Interest.*

Variable	Dapagliflozin (N=2373)		Placebo (N=2371)		Hazard or Rate Ratio or Difference (95% CI)	P Value
	values	*events/100 patient-yr*	*values*	*events/100 patient-yr*		
Efficacy outcomes						
Primary composite outcome — no. (%)†	386 (16.3)	11.6	502 (21.2)	15.6	0.74 (0.65 to 0.85)	<0.001
Hospitalization or an urgent visit for heart failure	237 (10.0)	7.1	326 (13.7)	10.1	0.70 (0.59 to 0.83)	NA
Hospitalization for heart failure	231 (9.7)	6.9	318 (13.4)	9.8	0.70 (0.59 to 0.83)	NA
Urgent heart-failure visit	10 (0.4)	0.3	23 (1.0)	0.7	0.43 (0.20 to 0.90)	NA
Cardiovascular death	227 (9.6)	6.5	273 (11.5)	7.9	0.82 (0.69 to 0.98)	NA
Secondary outcomes						
Cardiovascular death or heart-failure hospitalization — no. (%)	382 (16.1)	11.4	495 (20.9)	15.3	0.75 (0.65 to 0.85)	<0.001
Total no. of hospitalizations for heart failure and cardiovascular deaths‡	567	—	742	—	0.75 (0.65 to 0.88)	<0.001
Change in KCCQ total symptom score at 8 mo§	6.1±18.6	—	3.3±19.2	—	1.18 (1.11 to 1.26)	<0.001
Worsening renal function — no. (%)¶	28 (1.2)	0.8	39 (1.6)	1.2	0.71 (0.44 to 1.16)	NA
Death from any cause — no. (%)	276 (11.6)	7.9	329 (13.9)	9.5	0.83 (0.71 to 0.97)	NA

McMurray JJV et al. N Engl J Med 2019;381:1995-2008.

DAPA-HF Results

Subgroup	Dapagliflozin (N=2373)	Placebo (N=2371)	Hazard Ratio (95% CI)
	no. of patients/total no.		
All patients	386/2373	502/2371	0.74 (0.65–0.85)
Type 2 diabetes at baseline			
Yes	215/1075	271/1064	0.75 (0.63–0.90)
No	171/1298	231/1307	0.73 (0.60–0.88)

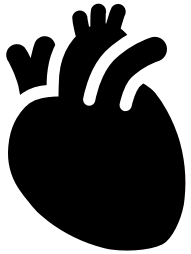


Conclusion: Among patients with HFrEF, the risk of worsening HF or death from cardiovascular causes was lower among those who received dapagliflozin than those who received placebo, **regardless of the presence or absence of diabetes**.

McMurray JJV et al. N Engl J Med 2019;381:1995-2008.

FDA grants Fast Track designation for Farxiga in heart failure

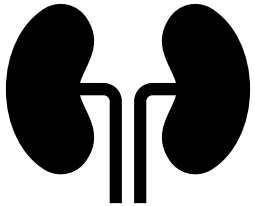
FDA has granted Fast Track designation for the development of *Farxiga* (dapagliflozin) to reduce the risk of cardiovascular (CV) death, or the worsening of heart failure, in adults with heart failure with reduced ejection fraction (HFrEF) or preserved ejection fraction (HFpEF).



Considerations for use in heart failure patients

Renal effects

- Acute kidney injury
- Chronic kidney disease





Volume status

- Volume depletion
- Diuretic use

Other concerns

- DKA
- Limb amputations
- GU infections



2016

FDA Drug Safety Communication: FDA strengthens kidney warnings for diabetes medicines canagliflozin (Invokana, Invokamet) and dapagliflozin (Farxiga, Xigduo XR)

2019

Newsroom – Published on: August 27, 2019

FDA Grants Fast Track Designation for Dapagliflozin to Prevent Kidney Failure

Acute Kidney Injury

Trial	SGLT2 inhibitor	Placebo	HR (95% CI)	p-value
EMPA-REG OUTCOME[1]	45/4687 (1.0%)	37/2333 (1.6%)	NA	NA
CANVAS Program[2,3] (event rate per 1000 patient-yr)	3.0	4.1	NA	0.33
History of HF	1.1	4.2	0.27 (0.02-2.95)	0.40
No history of HF	3.3	4.2	0.79 (0.40-1.56)	
DECLARE-TIMI 58[4]	125/8574 (1.5%)	175/8569 (2.0%)	0.69 (0.55-0.87)	0.002
CREDENCE[5]	86/2200 (3.9%)	98/2197 (4.5%)	0.85 (0.64-1.13)	NA
DAPA-HF[6]	153/2368 (6.5%)	170/2368 (7.2%)	NA	0.36

1.Zinman B et al. N Engl J Med 2015;373:2117-28.
2.Neal B et al. N Engl J Med 2017;377:644-57.
3.Radholm K et al. Circulation. 2018;138:458-468.
4.Wiviott SD et al. N Engl J Med 2019;380:347-57.
5. Perkovic V et al. N Engl J Med 2019;380:2995-306.
6. McMurray JJV et al. N Engl J Med 2019;381:1995-2008

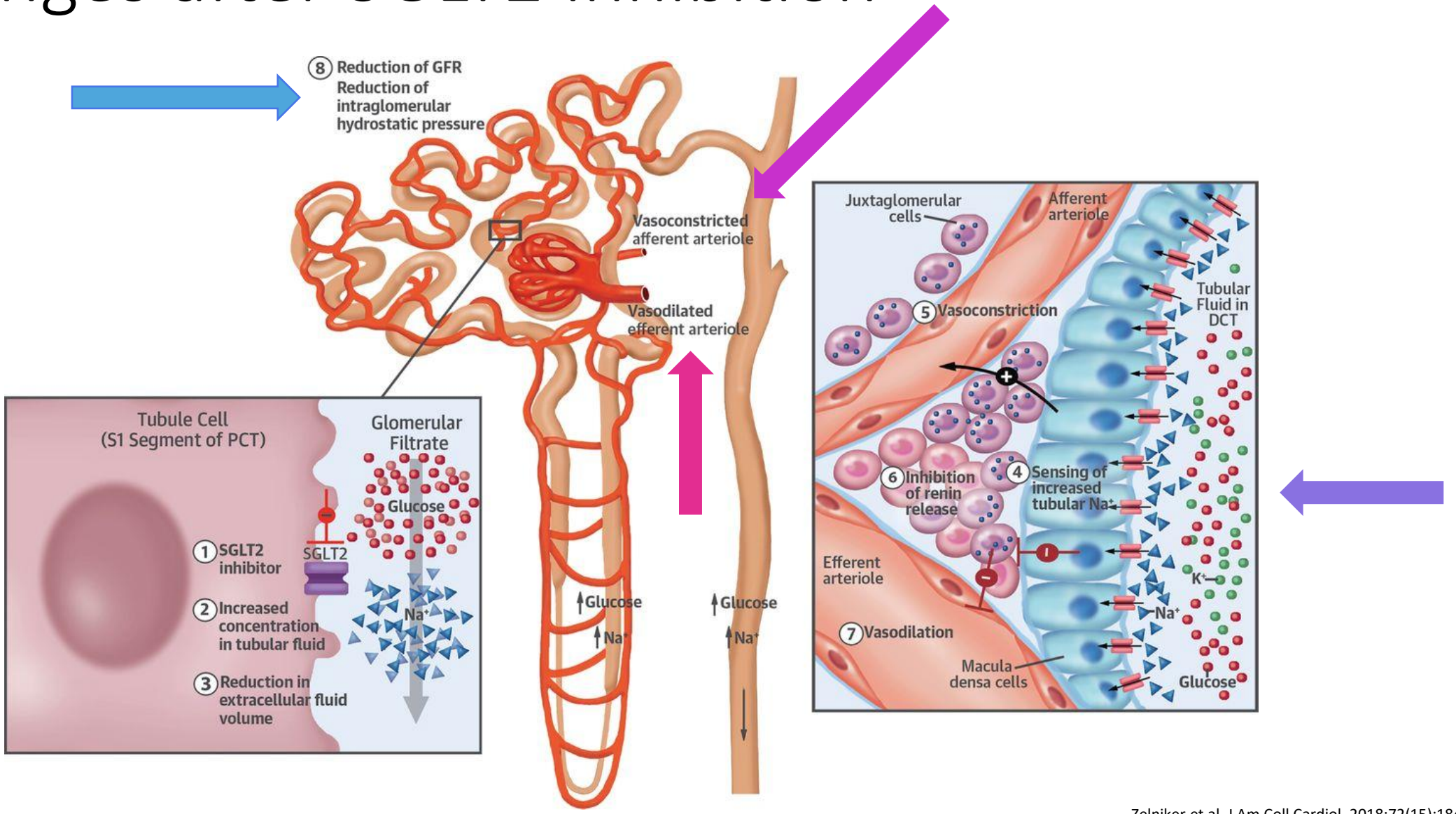
Acute Kidney Injury

- Expect transient changes upon initiation of SGLT2i therapy
  - Decrease in eGFR by ~3 to 4 mL/min/1.73m^2
- Changes in eGFR are likely **nephroprotective** over time

WHEN URINE LOVE

Vardeny et al. J Am Coll Cardiol HF 2019;7:169-72.

Changes after SGLT2 Inhibition



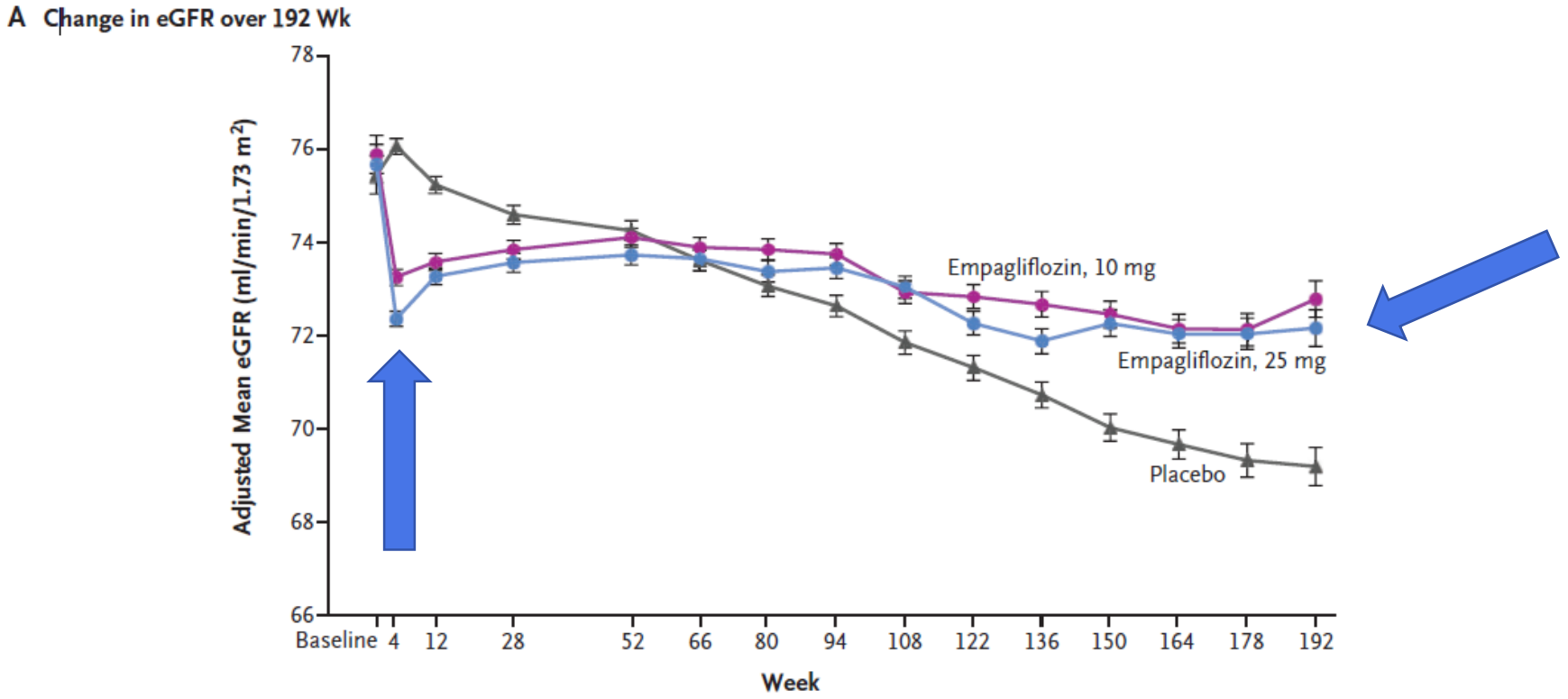
Zelniker et al. J Am Coll Cardiol. 2018;72(15):1845-55.

Renal Composite Outcomes

Trial	eGFR inclusion criteria	Renal composite outcome	SGLT2 inhibitor	Placebo	HR (95% CI)
EMPA-REG OUTCOME[1]	≥30	Doubling of SCr with eGFR ≤45, initiation of RRT, or death from renal disease	525/4124 (12.7%)	388/2061 (18.8%)	0.61 (0.53-0.70)
CANVAS Program[2,3] (event rate per 1000 patient-yrs)	≥30	40% reduction in eGFR, renal replacement therapy, or renal death	5.5	9.0	0.60 (0.47-0.77)
		Prior HF *No prior HF*	6.8 5.4	11.0 8.7	0.67 (0.30-1.51) 0.52 (0.37-0.72)
DECLARE-TIMI 58[4,5]	≥60	≥40% decrease in eGFR to <60, new ESRD, or death from renal causes	127/8582 (1.5%)	238/8578 (2.8%)	0.53 (0.43-0.66)
		Prior HF *No prior HF*	27/852 (3.2%) 100/7730 (1.3%)	48/872 (5.5%) 190/7706 (2.5%)	0.58 (0.36-0.92) 0.52 (0.41-0.66)

1. Wanner C et al. N Engl J Med 2016;375:323-34..
2. Neal B et al. N Engl J Med 2017;377:644-57.
3. Radholm K et al. Circulation. 2018;138:458-468.
4. Wiviott SD et al. N Eng J Med 2019;380:347-57.
5. Mosenzon O et al. Lancet Diabetes Endocrinol. 2019;7:606-17.

Renal Outcomes in EMPA-REG OUTCOME

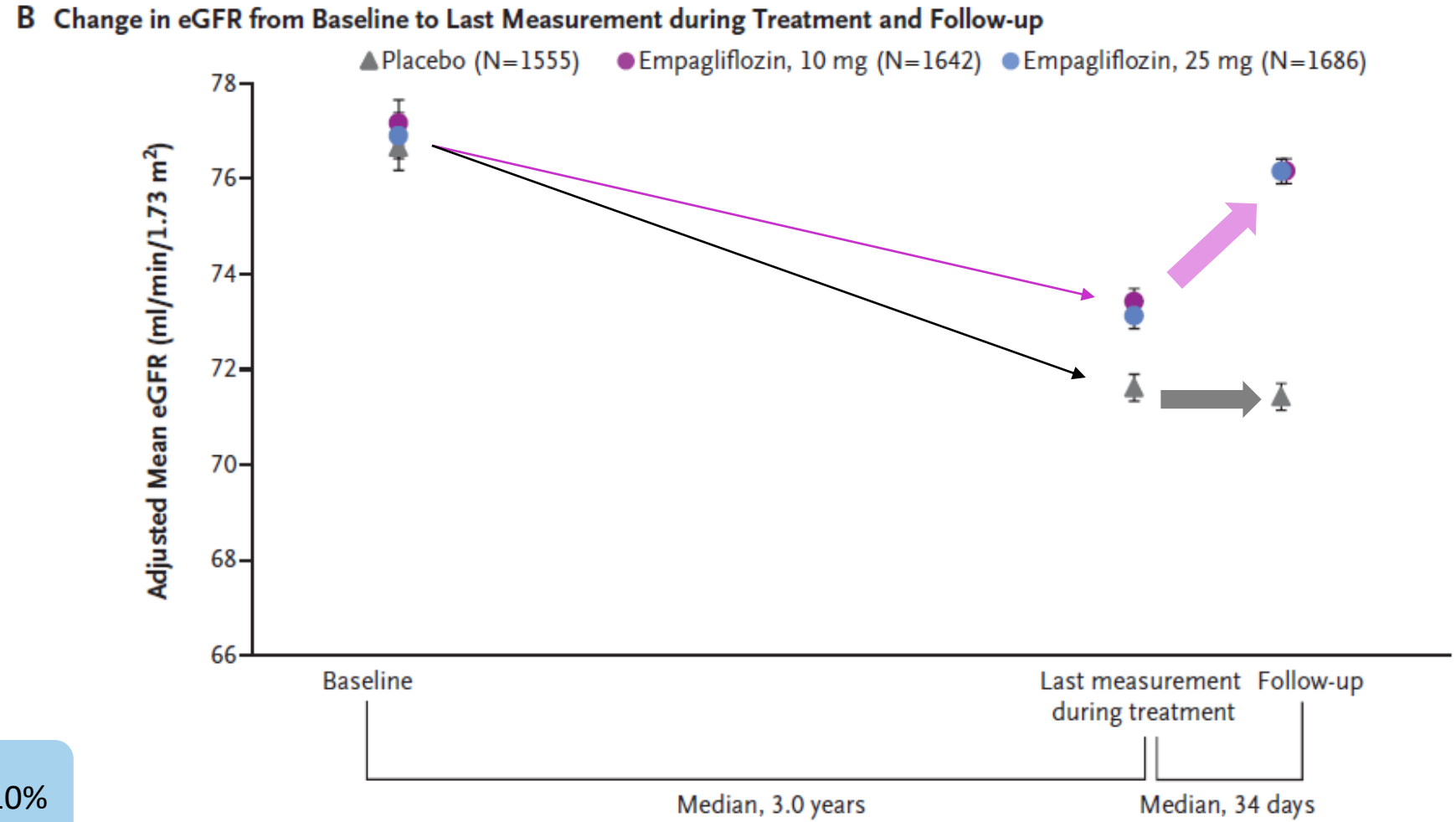


No. at Risk															
Placebo	2323	2295	2267	2205	2121	2064	1927	1981	1763	1479	1262	1123	977	731	448
Empagliflozin, 10 mg	2322	2290	2264	2235	2162	2114	2012	2064	1839	1540	1314	1180	1024	785	513
Empagliflozin, 25 mg	2322	2288	2269	2216	2156	2111	2006	2067	1871	1563	1340	1207	1063	838	524
No. in Follow-up Analysis															
Total	7020	7020	6996	6931	6864	6765	6696	6651	6068	5114	4443	3961	3488	2707	1703

HF at baseline: 10%

Wanner C et al. N Engl J Med 2016;375:323-34.

Renal Outcomes in EMPA-REG OUTCOME



HF at baseline: 10%

Wanner C et al. N Engl J Med 2016;375:323-34.

Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy (CREDENCE)

Study Design	Double-blind, randomized, event-driven trial
Methods	Canagliflozin 100 mg once daily or placebo
Inclusion Criteria	At least 30 years of age with type 2 diabetes and CKD [eGFR 30-89 mL/min/1.73m^2 and albuminuria (UACR >300 to 5000)]; on a stable dose of an ACEi/ARB for at least 4 weeks
Exclusion Criteria	Use of a direct renin inhibitor or **mineralcorticoid-receptor antagonist** Non-diabetic kidney disease, type 1 DM, treated with immunosuppression for kidney disease, a history of dialysis or kidney transplant
Primary Endpoint	Composite of end-stage kidney disease (dialysis for at least 30 days, kidney transplant, or eGFR<15 mL/min/1.73m^2 sustained for at least 30 days), doubling of the serum creatinine level from baseline sustained for at least 30 days, or death from renal or cardiovascular disease

Perkovic V et al. N Engl J Med 2019;380:2995-306.

CREDENCE Results

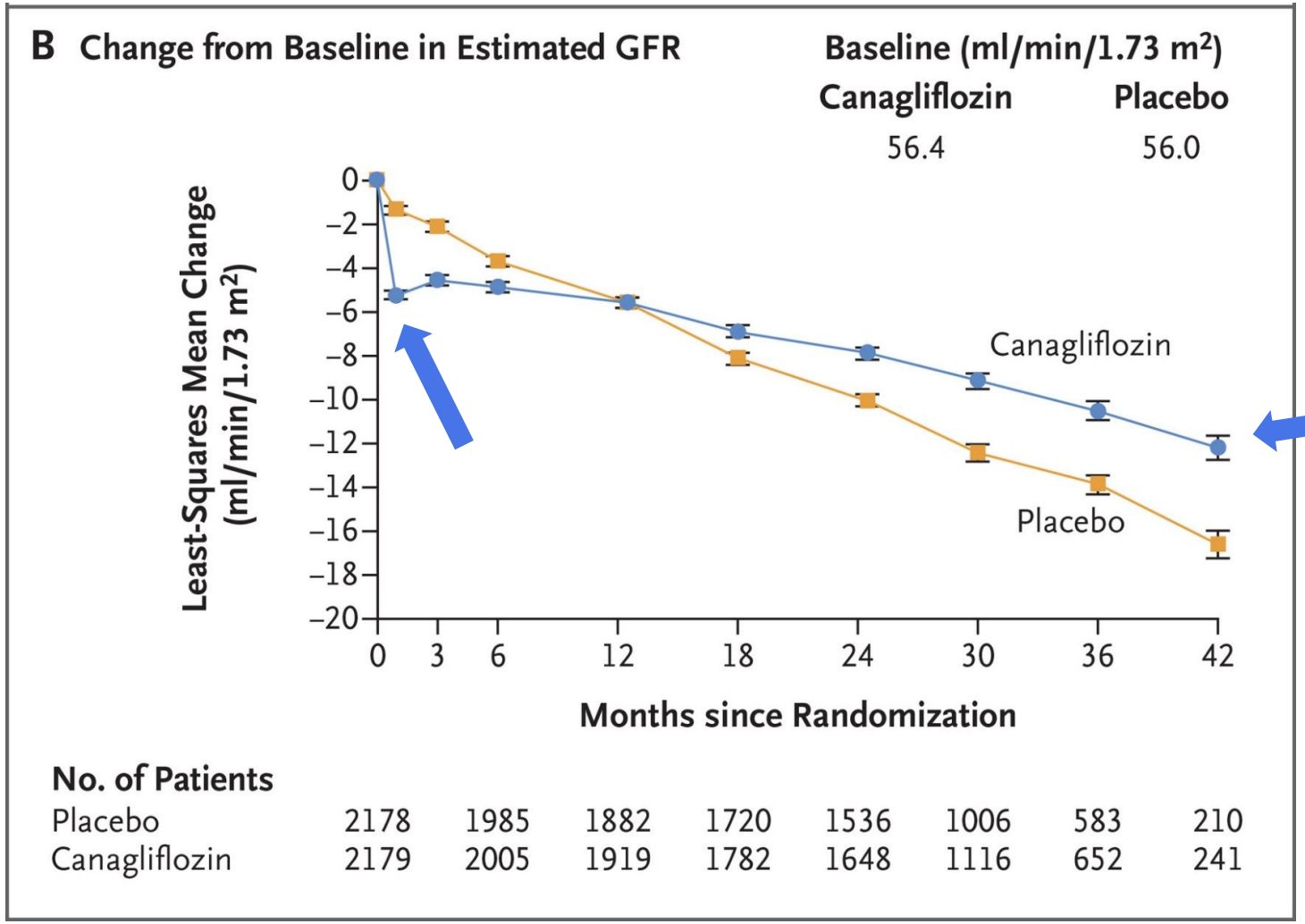
HF at baseline:
652/4401 (14.8%)

Outcomes	Canagliflozin (n=2202)	Placebo (n=2199)	HR (95% CI)	p-value
Primary composite outcome	245	340	0.70 (0.59-0.82)	0.00001
Doubling of SCr	118	188	0.60 (0.48-0.76)	<0.001
End-stage kidney disease	116	165	0.68 (0.54-0.86)	0.002
eGFR <15	78	125	0.60 (0.45-0.80)	NA
Dialysis or kidney transplant	76	100	0.74 (0.55-1.00)	NA
Renal death	2	5	NA	NA
CV death	110	140	0.78 (0.61-1.00)	0.05
Hospitalization for HF	89	141	0.61 (0.47-0.80)	<0.001

Perkovic V et al. N Engl J Med 2019;380:2995-306.

CREDENCE Results

HF at baseline: 14.8%



Perkovic V et al. N Engl J Med 2019;380:2995-306.

DAPA-HF Results

Worsening renal function:

Sustained ≥50% reduction in eGFR, ESRD, or death from renal causes

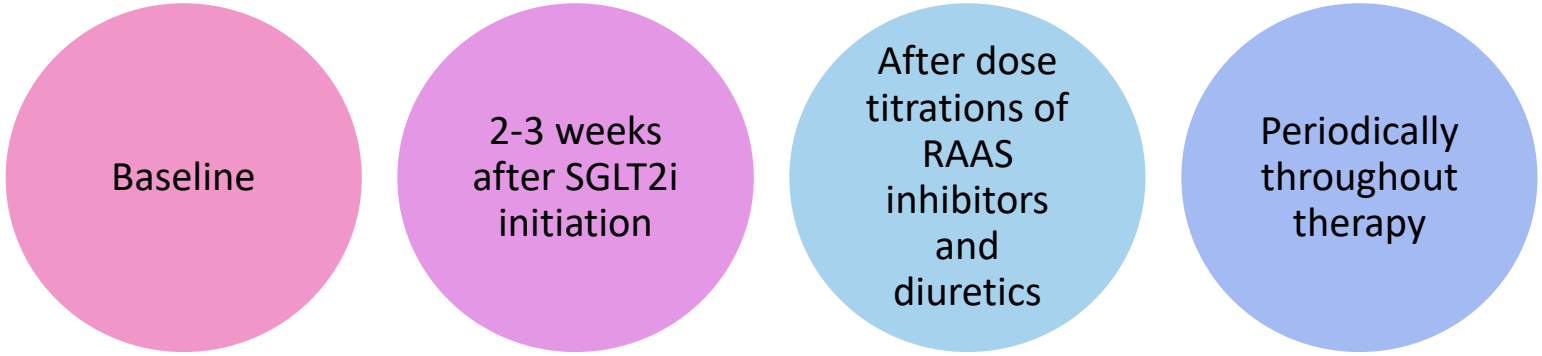
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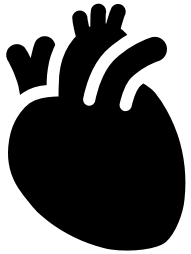
McMurray JJV et al. N Engl J Med 2019;381:1995-2008.

Management of Renal Effects in HF Patients

- Avoid SGLT2 inhibitors in patients with eGFR <30 mL/min/1.73m^2
- Prioritize ACEi/ARB dose optimization prior to adding an SGLT2i
- Expect a decrease in eGFR by ~3 to 4 mL/min/1.73m^2 initially
- Long-term benefits likely outweigh the risks of an acute change
- Proposed renal function monitoring:



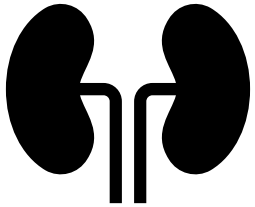
Vardeny et al. J Am Coll Cardiol HF 2019;7:169-72.



Considerations for use in heart failure patients

Renal effects

- Acute kidney injury
- Chronic kidney disease





Volume status

- Volume depletion
- Diuretic use

Other concerns

- DKA
- Limb amputations
- GU infections



Volume Depletion

- Mechanism of volume depletion:
  - Osmotic diuresis
  - Natriuresis
- Increases in urine output (UOP) initially
  - Return to baseline after several weeks
- Potential for dehydration, hypovolemia, and orthostatic hypotension, especially in patients on diuretic therapy

Hallow KM. Diabetes Obes Metab. 2018;20:479-487.

Baseline Diuretic Use

Trial	SGLT2 inhibitor	Placebo
EMPA-REG OUTCOME		
Total[1]	725/4687 (15.5%)	364/2333 (15.6%)
With HF[2]	224/462 (48.5%)	110/244 (45.1%)
Without HF[2]	501/4225 (11.9%)	254/2089 (12.2%)
CANVAS Program[3]		
Total	716/5795 (12.3%)	592/4347 (13.6%)
With HF	201/803 (25.0%)	178/658 (27.1%)
Without HF	515/4992 (10.3%)	414/3689 (11.2%)
DECLARE-TIMI 58[4]	3488/8582 (40.6%)	3479/8578 (40.6%)
CREDENCE[5]	1026 (46.6%)	1031 (46.9%)

1. Wanner C et al. N Engl J Med 2016;375:323-34..
2. Fitchett D et al. Euro Heart J. 2016;37:1526-1534.
3. Radholm K et al. Circulation. 2018;138:458-468.
4. Wiviott SD et al. N Eng J Med 2019;380:347-57.
5. Perkovic V. N Engl J Med 2019;380:2295-306.

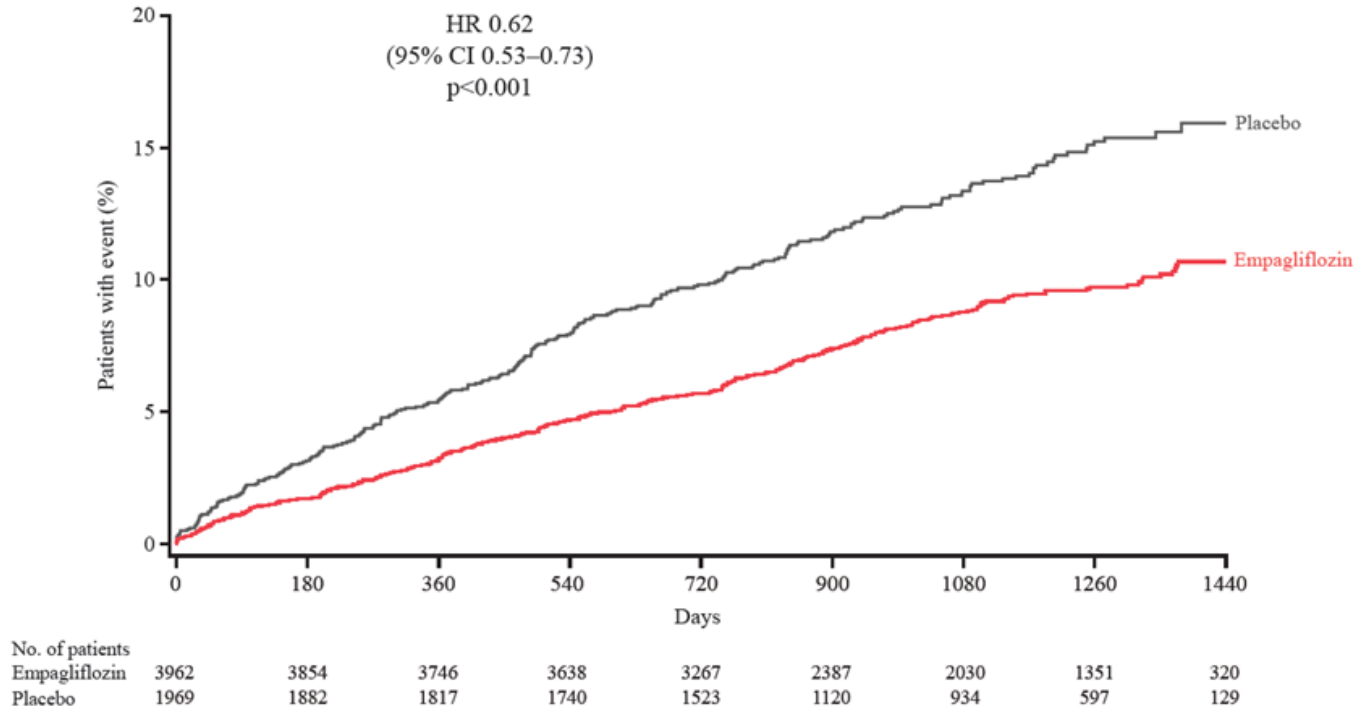
Volume Depletion Events

Trial	SGLT2 inhibitor	Placebo	HR (95% CI)	p-value
EMPA-REG OUTCOME[1]	239/4687 (5.1%)	115/2333 (4.9%)	NA	NA
On loop diuretics[2]	135/239 (56.5%)	67/115 (58.3%)		
CANVAS Program[3,4]	26.0	18.5	NA	0.009
(events per 1000 patient-yr)				
History of HF	21.2	14.9	1.69 (0.67-4.26)	1.00
No history of HF	28.0	19.7	1.44 (1.07-1.92)	
DECLARE-TIMI 58[5]	213/8574 (2.5%)	207/8569 (2.4%)	1.00 (0.83-1.21)	0.99
On loop diuretics[6]	57/866 (6.6%)	57/934 (6.1%)	NA	NA
CREDENCE[7]	144/2200 (6.5%)	115/2197 (5.2%)	1.25 (0.97-1.59)	NA

1. Zinman B et al. N Engl J Med 2015;373:2117-28.
2. Wanner C et al. N Engl J Med 2016;375:323-34..
3. Neal B et al. N Engl J Med 2017;377:644-57..
4. Radholm K et al. Circulation. 2018;138:458-468.
5. Wiviott SD et al. N Eng J Med 2019;380:347-57.
6. Mosenzon O et al. Lancet Diabetes Endocrinol. 2019;7:606-17.
7. Perkovic V et al. N Engl J Med 2019;380:2995-306.

Loop Diuretic Introduction in EMPA-REG OUTCOME

Empagliflozin	Placebo
340/3962 (8.6%)	262/1969 (13.3%)



Time to first introduction of loop diuretics

HF at baseline: 10%

Fitchett D et al. Euro Heart J. 2016;37:1526-1534.

Volume Depletion Events in DAPA-HF

Outcome	Dapagliflozin (n=2368)	Placebo (n=2368)
Baseline loop diuretic use	2216 (93.4%)	2217 (93.5%)
Volume depletion event	178 (7.5%)	162 (6.8%)
Hypotension	94 (4.0%)	84 (3.5%)
Dehydration	35 (1.5%)	29 (1.2%)
Hypovolemia	34 (1.4%)	23 (1.0%)
Syncope	13 (0.5%)	22 (0.9%)
Orthostatic hypotension	12 (0.5%)	10 (0.4%)
BP decreased	4 (0.2%)	1 (0.0%)
Shock/circulatory collapse	2 (0.1%)	8 (0.3%)

McMurray JJV et al. N Engl J Med 2019;381:1995-2008.

Management of Volume Depletion

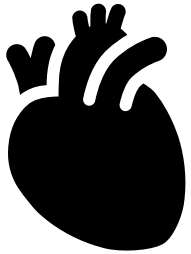
Assess volume status

- Initiate SGLT2 inhibitor when patient is **euvolemic** or hypervolemic
- Consider empiric reduction of loop diuretic dose when initiating SGLT2 inhibitor
  - Proposed loop diuretic dose reduction of 50%
  - Reassess within 3 to 4 weeks

Patient education

- Maintain adequate hydration
- Daily weight and blood pressure monitoring

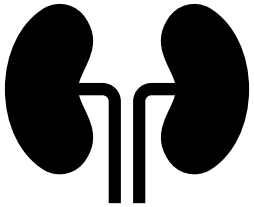
Triantafylidis et al. J Pharm Pract. 2019;20:1-10.
Vardeny et al. J Am Coll Cardiol HF. 2019;7:169-72.



Considerations for use in heart failure patients

Renal effects

- Acute kidney injury
- Chronic kidney disease





Volume status

- Volume depletion
- Diuretic use

Other concerns

- DKA
- Limb amputations
- GU infections



Diabetic Ketoacidosis

- Cases of euglycemic ketoacidosis have been reported
- Incidence of diabetic ketoacidosis (DKA) in trials:

Trial	SGLT2 inhibitor	Placebo
EMPA-REG OUTCOME[1]	4	1
CANVAS[2]	12	6
DECLARE-TIMI 58[3]	27	12
CREDENCE[4]	11	1
DAPA-HF[5]	3	0

- Should we be concerned in patients **without** diabetes?

1. Zinman B et al. N Engl J Med 2015;373:2117-28.
2. Neal B et al. N Engl J Med 2017;377:644-57.
3. Wiviott SD et al. N Engl J Med 2019;380:347-57.
4. Perkovic V et al. N Engl J Med 2019;380:2995-306.
5. McMurray JJV et al. N Engl J Med 2019;381:1995-2008.

DKA Considerations in HF Patients

- Consider risk factors in patients *with or without* DM



- Hold SGLT2i for at least 24 hours prior to events that may precipitate ketoacidosis or during periods of illness and stress

Vardeny et al. J Am Coll Cardiol HF. 2019;7:169-72.

Other Potential Concerns with SGLT2 Inhibitors

Incidence in DAPA-HF	Dapagliflozin	Placebo
Urinary tract infections	11	17
Genital infections	0	0
Fournier's gangrene	0	1
Limb amputation	13	12

McMurray JJV et al. N Engl J Med 2019;381:1995-2008.

Other Potential Concerns with SGLT2 Inhibitors

Urinary tract infections	Responsive to typical treatment
Genital infections	Prevent with proper hygiene
Fournier's gangrene	Extremely rare
Limb amputation	Potentially a concern in patients with severe PAD or foot wounds at baseline

Vardeny et al. J Am Coll Cardiol HF. 2019;7:169-72.

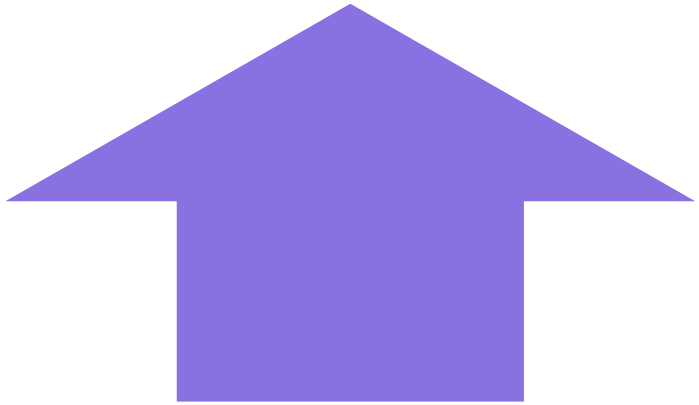


Favorable

- Reduce preload
- Reduce afterload
- Delay CKD progression
- Glucose control (if needed)

Unfavorable

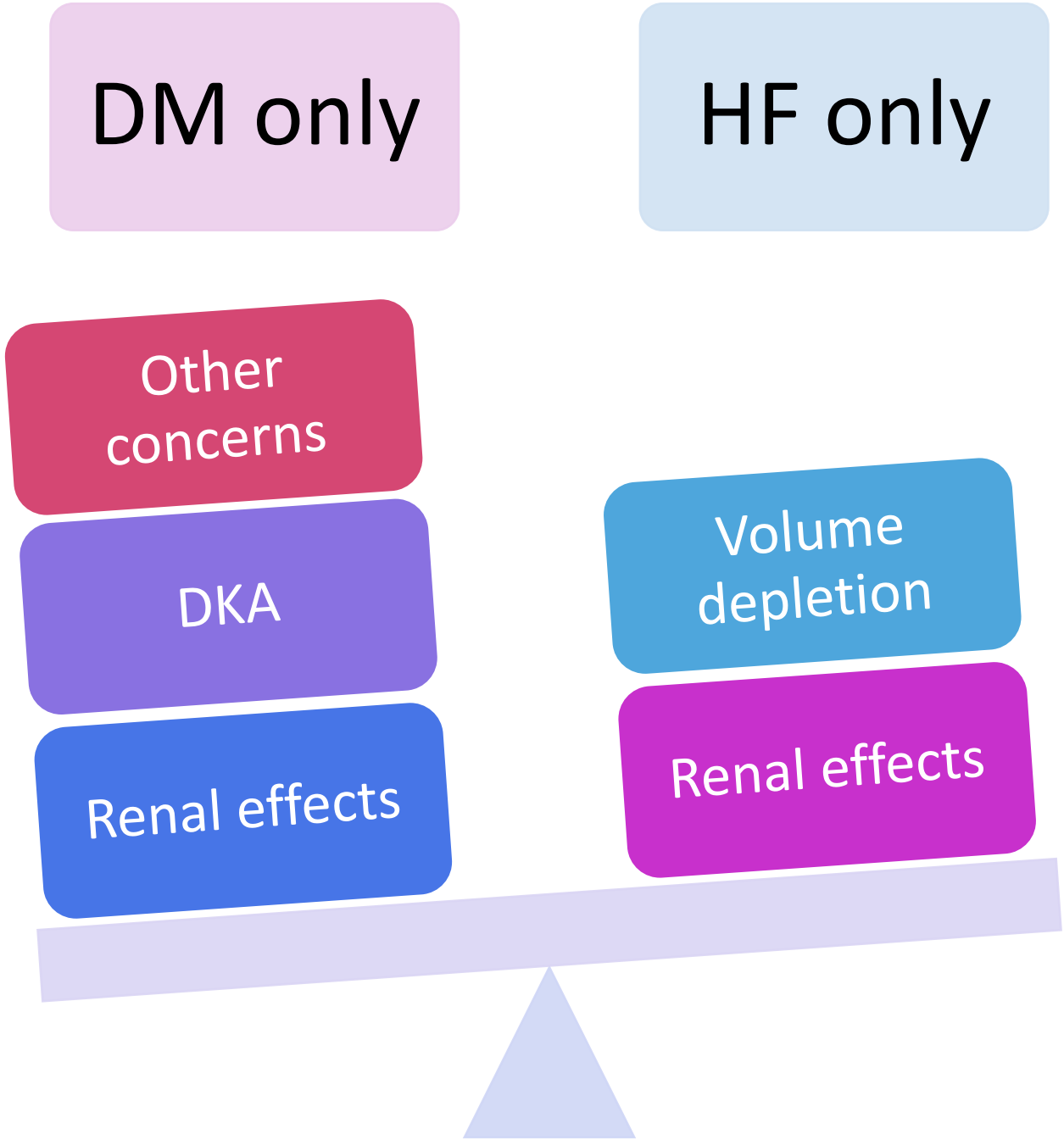
- Volume depletion
- DKA
- Genourinary tract infection
- Limb amputations



Zelniker TA et al. J Am Coll Cardiol. 2018;72(15):1845-55.

Solving the Controversy…

Are SGLT2 inhibitors safe in heart failure patients?


DM only
HF only
Other concerns
DKA
Renal effects
Volume depletion
Renal effects

Are SGLT2 inhibitors safe in heart failure patients?

SGLT2 inhibitors may be *safer* to use in heart failure patients, without diabetes. Appropriate monitoring and follow-up is **essential** to mitigate potential adverse reactions.

Initiating SGLT2 Inhibitor Therapy

Multidisciplinary care

Patient education

Provider education

Frequent monitoring

Stable patients in an ambulatory setting

Prioritize GDMT prior to initiating SGLT2i therapy

Assess volume status

Establish baseline renal function

Monitoring SGLT2 Inhibitor Therapy

Daily

- Weight
- Blood pressure

2-3 weeks

- Renal function
- Loop diuretic use

Conclusions

SGLT2 inhibitors have demonstrated a benefit in reducing heart failure hospitalizations & may soon be used in HF management

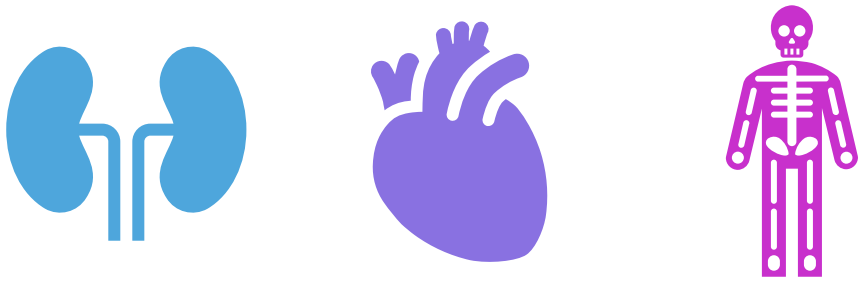
SGLT2 inhibitors are **safe** to use in patients with heart failure

Appropriate monitoring, patient and provider education, and multidisciplinary care is the safest and most effective way to utilize the benefits of SGLT2 inhibitors in heart failure

Questions?

SGLT2 Inhibitors in Heart Failure Management:

Risk Reduction or Risking it all?



Dominique Monteleone, PharmD

January 14, 2020