NA-GLUCOSE COTRANSPORTER 2 INHIBITORS (SGLT2i)

FLAME LECTURE: 7

NIKAMAL 9.21.18

OBJECTIVES

- To understand the mechanism of action of Na-Glucose Cotransporter 2 (SGLT2) inhibitors
- To counsel the patient regarding the benefits, risks, and uses for Na-Glucose Cotransporter 2 (SGLT2) inhibitors
- Prerequisites:
  - NONE
- See also – for closely related topics
  - FLAMEs on Type 2 DM / Medications for treatment of DM

AVAILABLE SGLT2 INHIBITORS

- FDA-Approved SGLT2i medications:
  - Canagliflozin (Invokana)
  - Dapagliflozin (Farxiga)
  - Empagliflozin (Jardiance)

MECHANISM OF ACTION

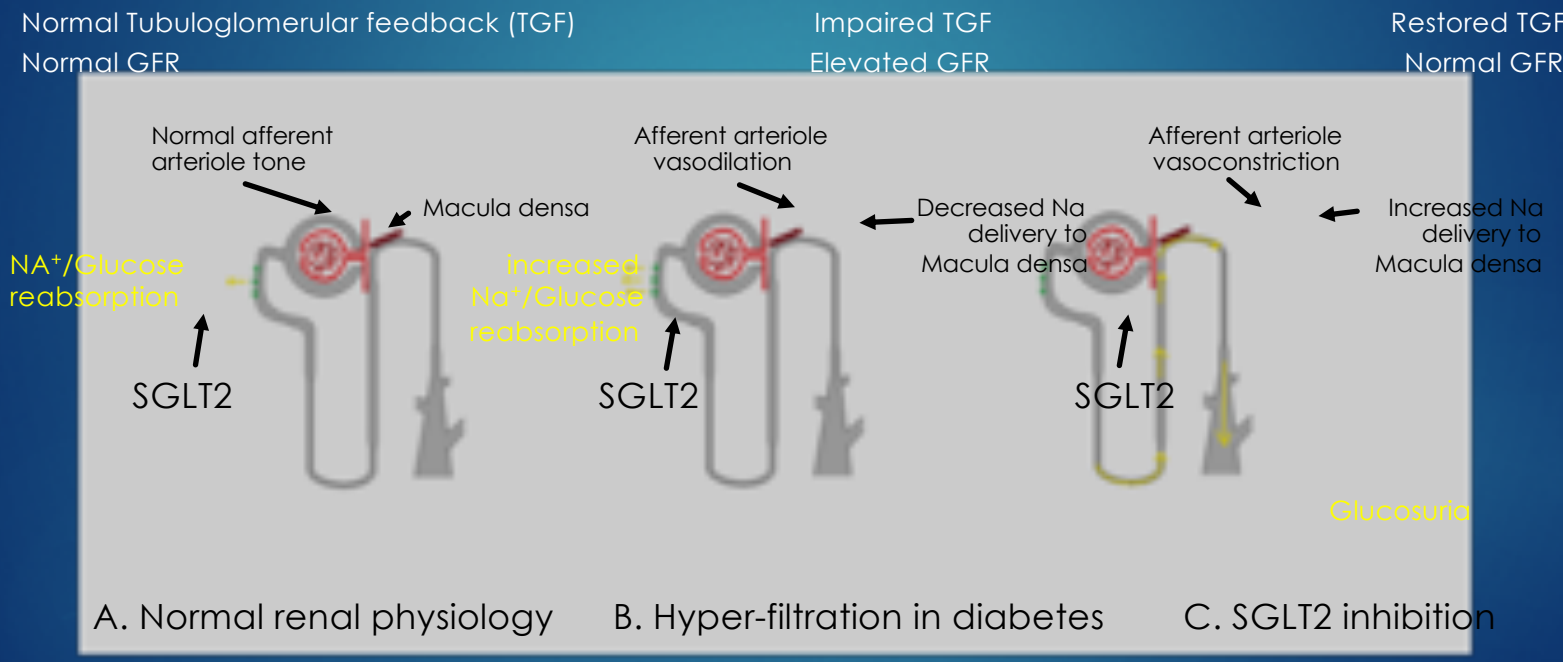

Illustration by Aimal Nikamal, MD. Adapted from Paola Fioretto et al. Dia Care 2016;39:S165-S171

INDICATIONS & CONTRAINDICATIONS

- FDA-Labeled Indications:
  - Type 2 Diabetes Mellitus
- Contra-indications:
  - Dialysis
  - Severe renal impairment estimated GFR < 30 ml/min/1.73 m(2)
  - Hypersensitivity to this class or components of medication
- Black-box warning:
  - Type 2 diabetic patients who have established cardiovascular disease (CVD) or at risk for CVD, these medications have been associated with lower limb amputations
  - Consider factors that increase risk of amputations and monitor for infections or ulcers of the lower limbs before initiation

SIDE EFFECTS

- Common:
  - Renal: Micturition frequency and polyuria
  - Reproductive: Genital infections (i.e vulvovaginal candidiasis)
- Serious:
  - Cardiovascular: Hypovolemia
  - Endocrine: Diabetic ketoacidosis, Hypoglycemia
  - Gastrointestinal: Pancreatitis
  - Immunologic: Hypersensitivity, Anaphylaxis
  - MSK: Fracture of bone
  - Renal: Acute kidney injury, Pyelonephritis
  - Other: Limb loss, Fournier's gangrene

REFERENCES

- The Na^+/Glucose Cotransporter Inhibitor Canagliflozin Activates AMPK by Inhibiting Mitochondrial Function and Increasing Cellular AMP Levels. Simon A. Hawley, Rebecca J. Ford, Brennan K. Smith, Graeme J. Gowans, Sarah J. Mancini, Ryan D. Pitt, Emily A. Day, Ian P. Salt, Gregory R. Steinberg, D. Grahame Hardie Diabetes Sep 2016, 65 (9) 2784-2794; DOI: 10.2337/db16-0058
- Canagliftozin. Micromedex solutions. Truven Health Analytics, Inc. Ann arbor, MI. Available at http://www.micromedexsolutions.com. Accessed September 14, 2018.
- Paola Fioretto et al. Dia Care 2016;39:S165-S171