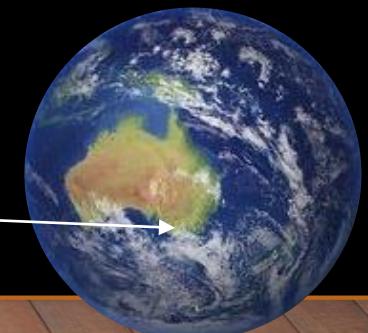


VERTIS-CV IS IT ALL CLASS?

Mark Cooper
from here —



CONFLICT OF INTEREST

I have received honoraria for medical educational meetings conducted on behalf of pharmaceutical companies including: Merck/MSD, Lilly, Boehringer-Ingelheim, Astra Zeneca, Novartis and Servier

I have attended advisory boards of pharmaceutical companies including: Boehringer-Ingelheim, Astra Zeneca, Merck/MSD, MundiPharma and Reata.

I have received research support from Boehringer-Ingelheim & Novo

WHAT IS CLASS?

Things regarded as high-quality,
integrity, status, or style

“a class act”

VERTIS-CV



WHAT IS A DRUG CLASS ?

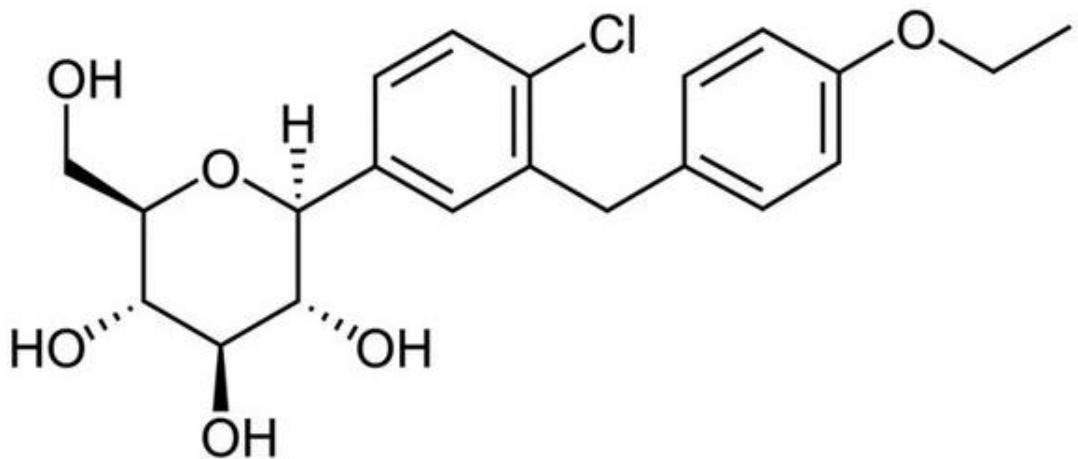
Drugs that share scientifically documented properties :

Chemical Structure SGLT2 inhibitors

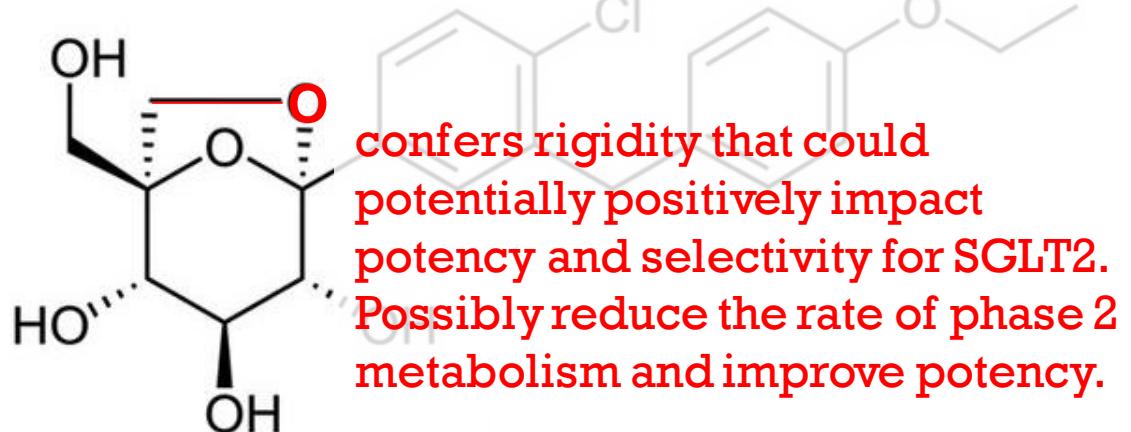
Mechanism of Action SGLT2 inhibitors

Physiological Effect SGLT2 inhibitors

SPOT THE DIFFERENCE?

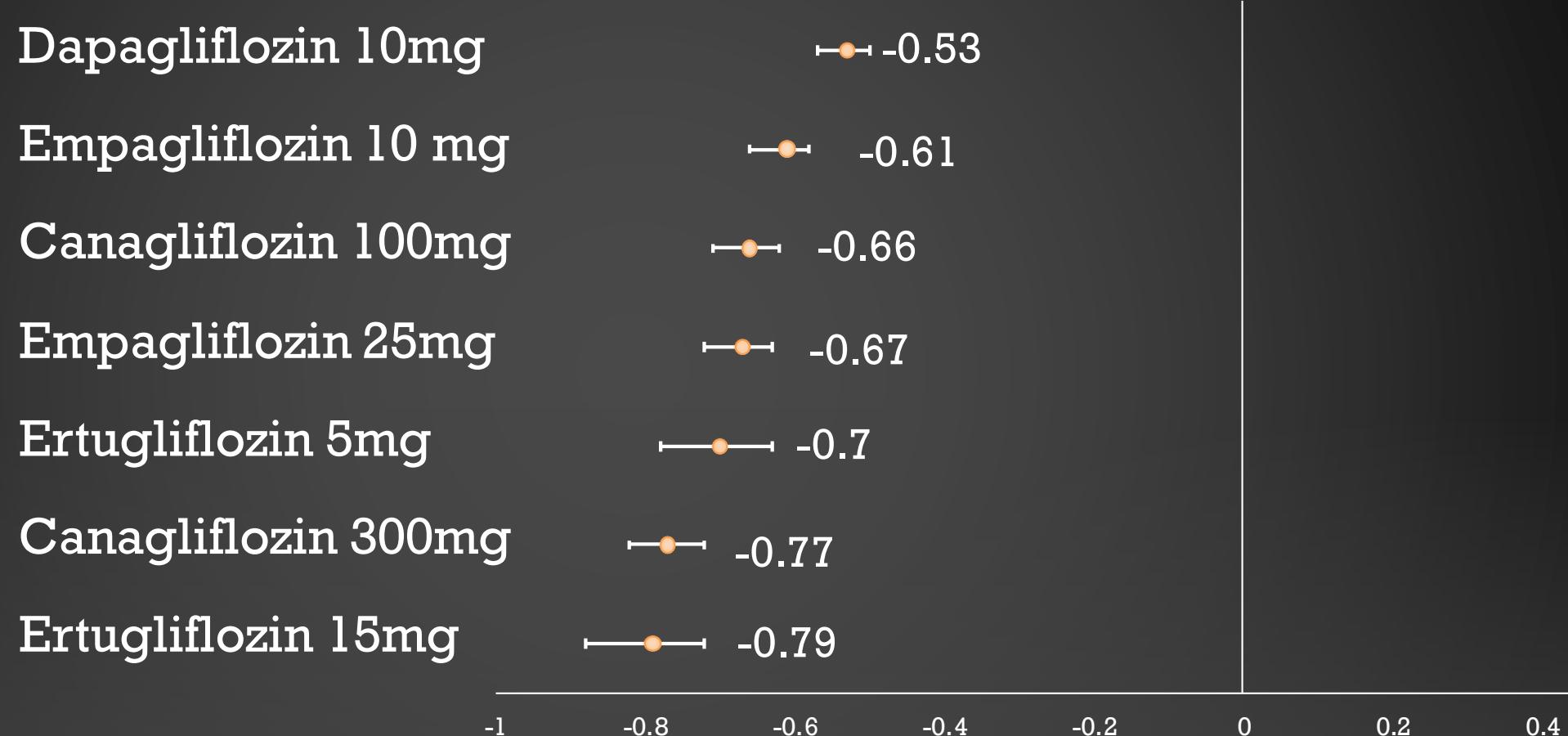


bridged ketal motif



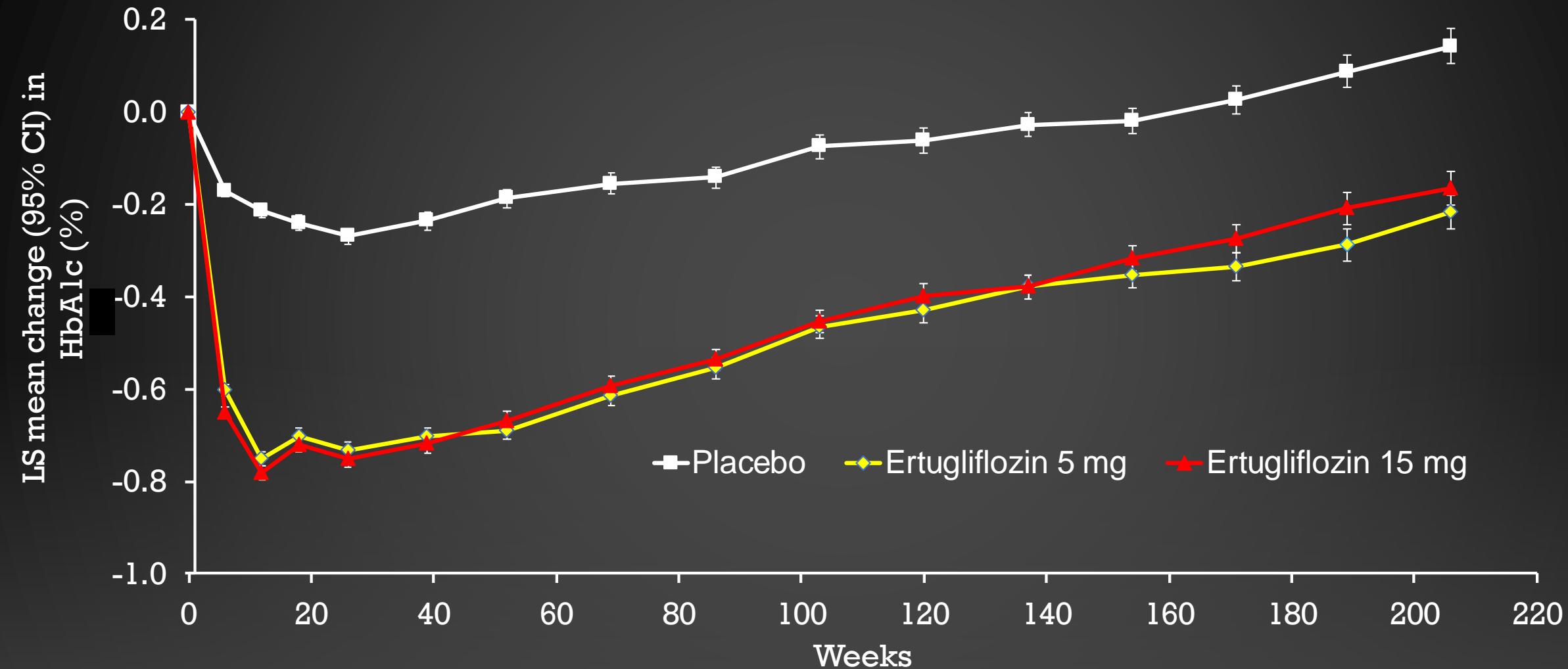
	SGLT2 IC ⁵⁰ (nM)	SGLT1 IC ⁵⁰ (nM)	(SGLT2:SGLT1)
Dapagliflozin	1.2	1400	~ 1200-fold
Ertugliflozin	0.877	1960	~ 2200-fold

SPOT THE DIFFERENCE?



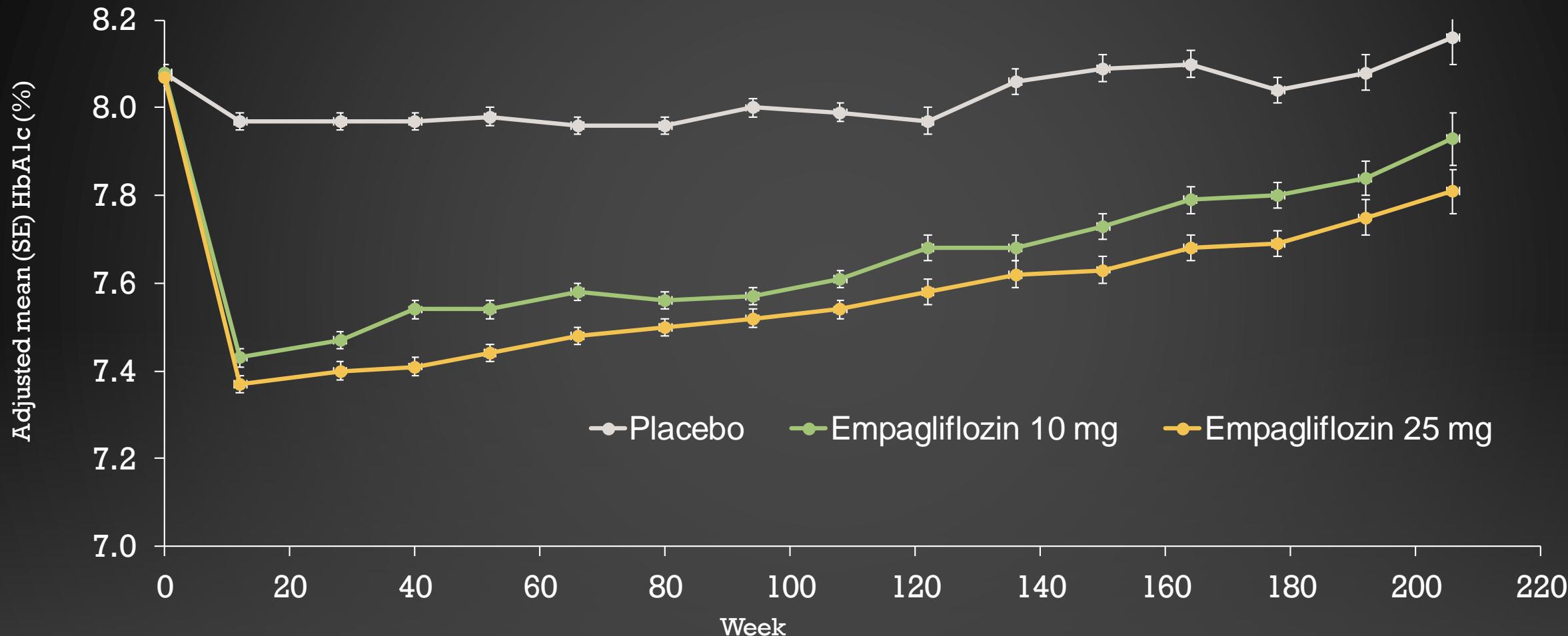
Predicted HbA1c response (95% CI) at 26 weeks on background oral treatment baseline HbA1c 8.0% and eGFR = 90ml/min/1.73m²

VERTIS-CV Change in HbA1c over time

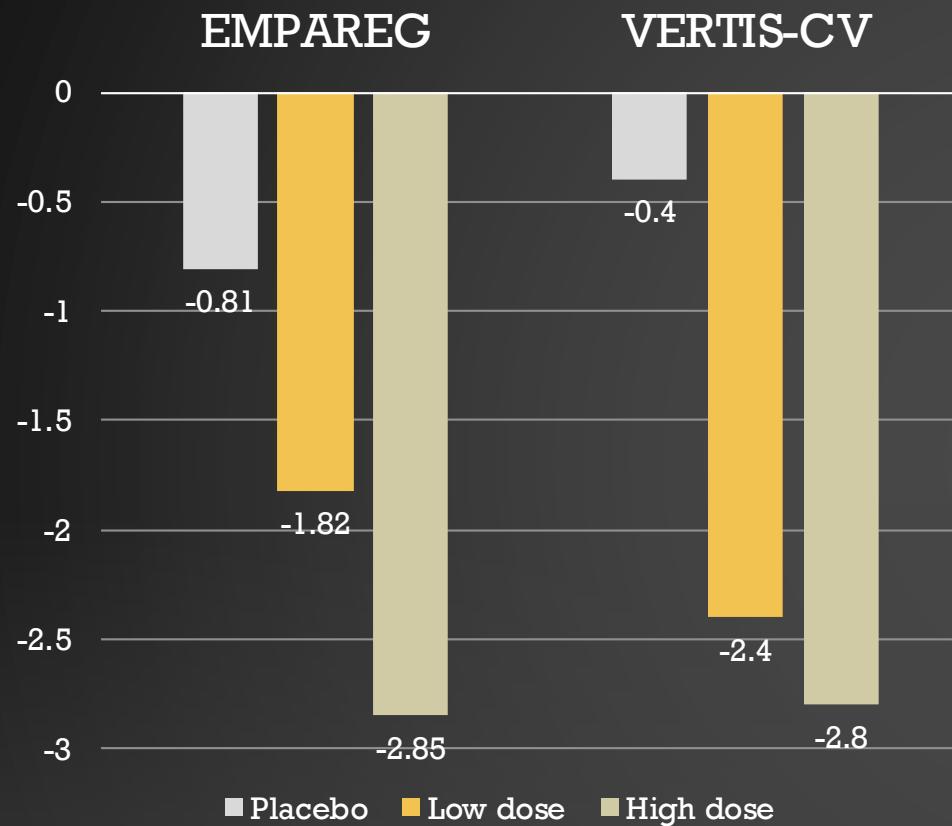


Doses of background antihyperglycemic medication were held constant for the initial 18 weeks of the study except for those patients meeting the glycemic rescue criteria.
CI, confidence interval; HbA1c, glycated hemoglobin; LS, least squares.

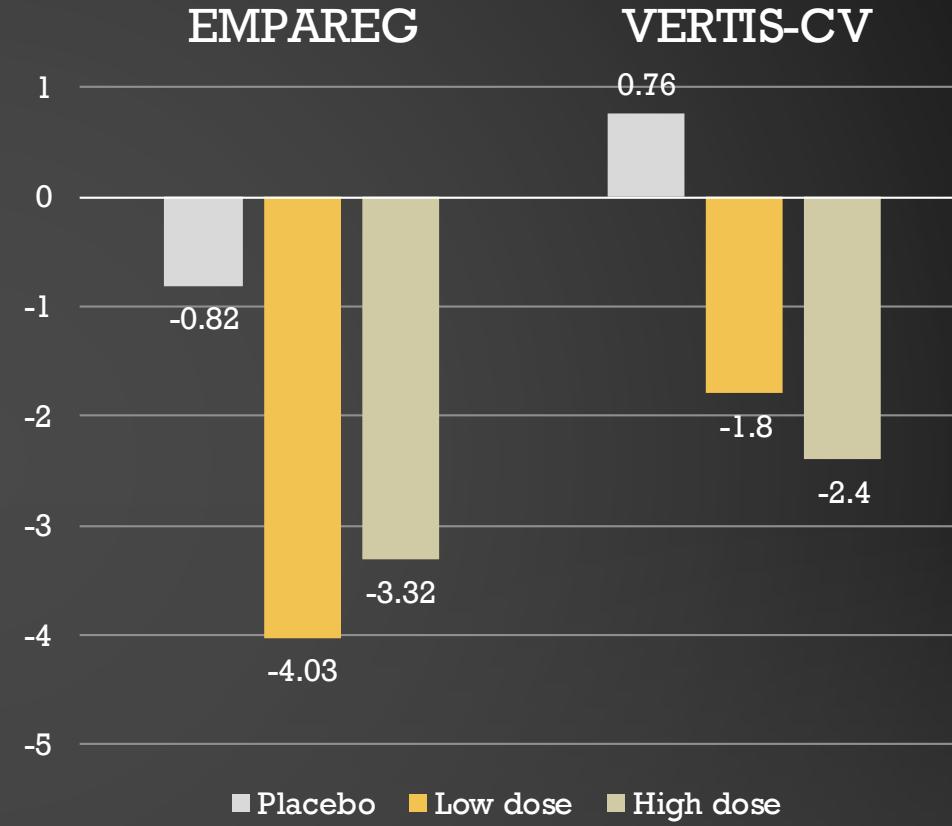
EMPA-REG Outcomes Change in HbA1c over time



SPOT THE DIFFERENCE?

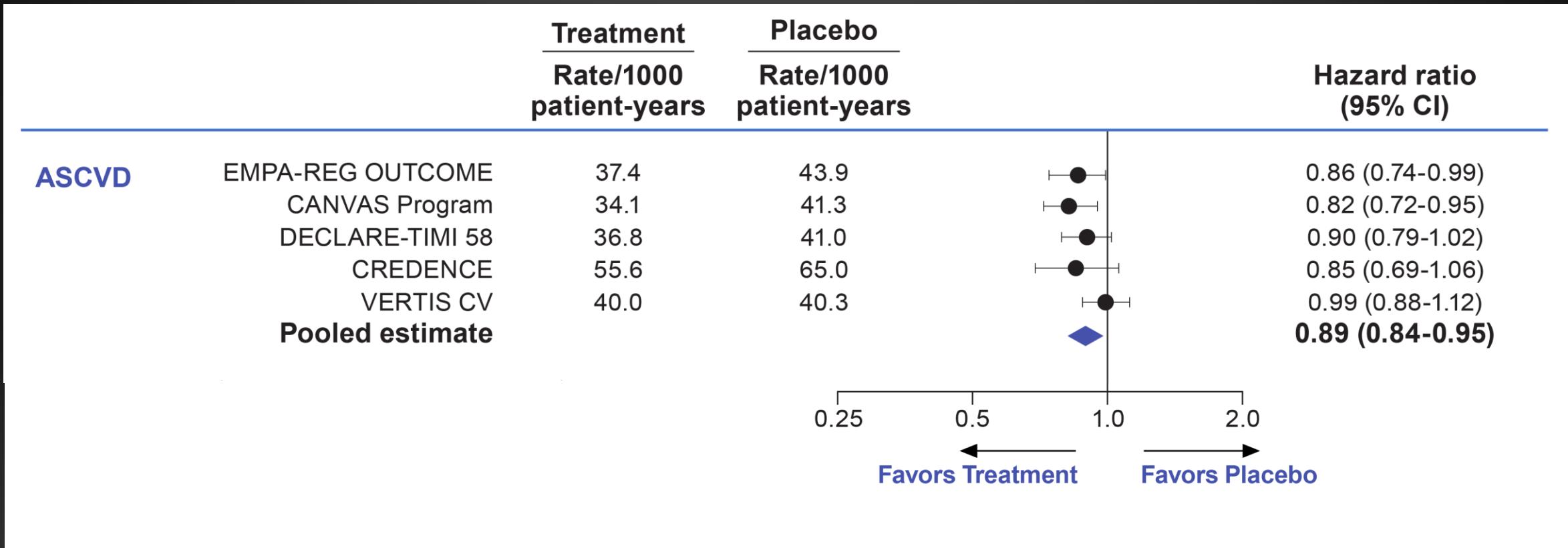


Weight loss*



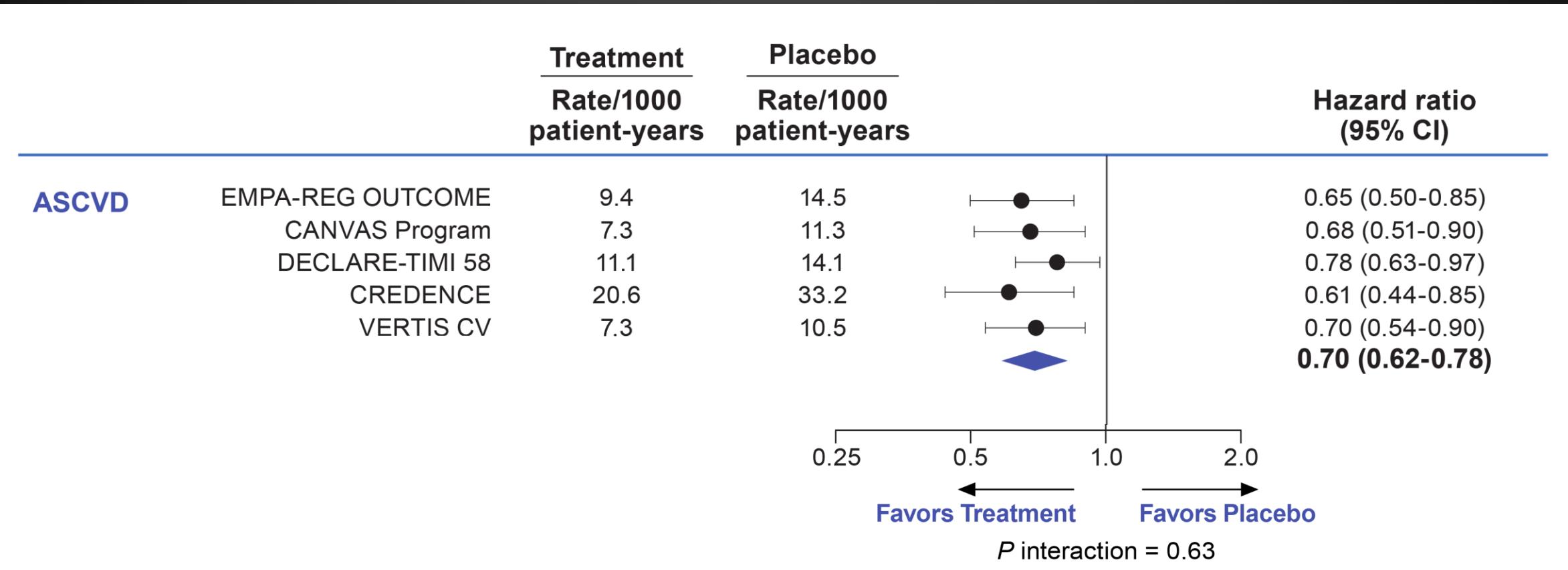
Lower SBP*

TIME TO FIRST MACE IN PATIENTS WITH ASCVD

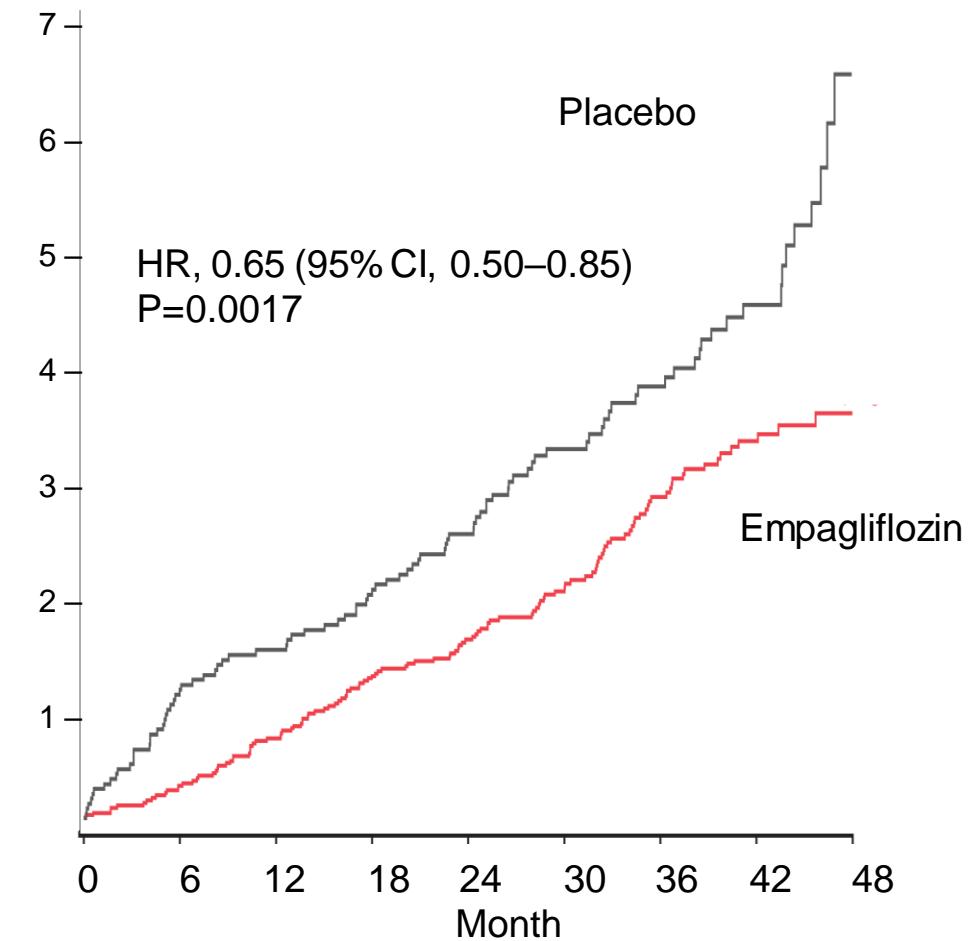
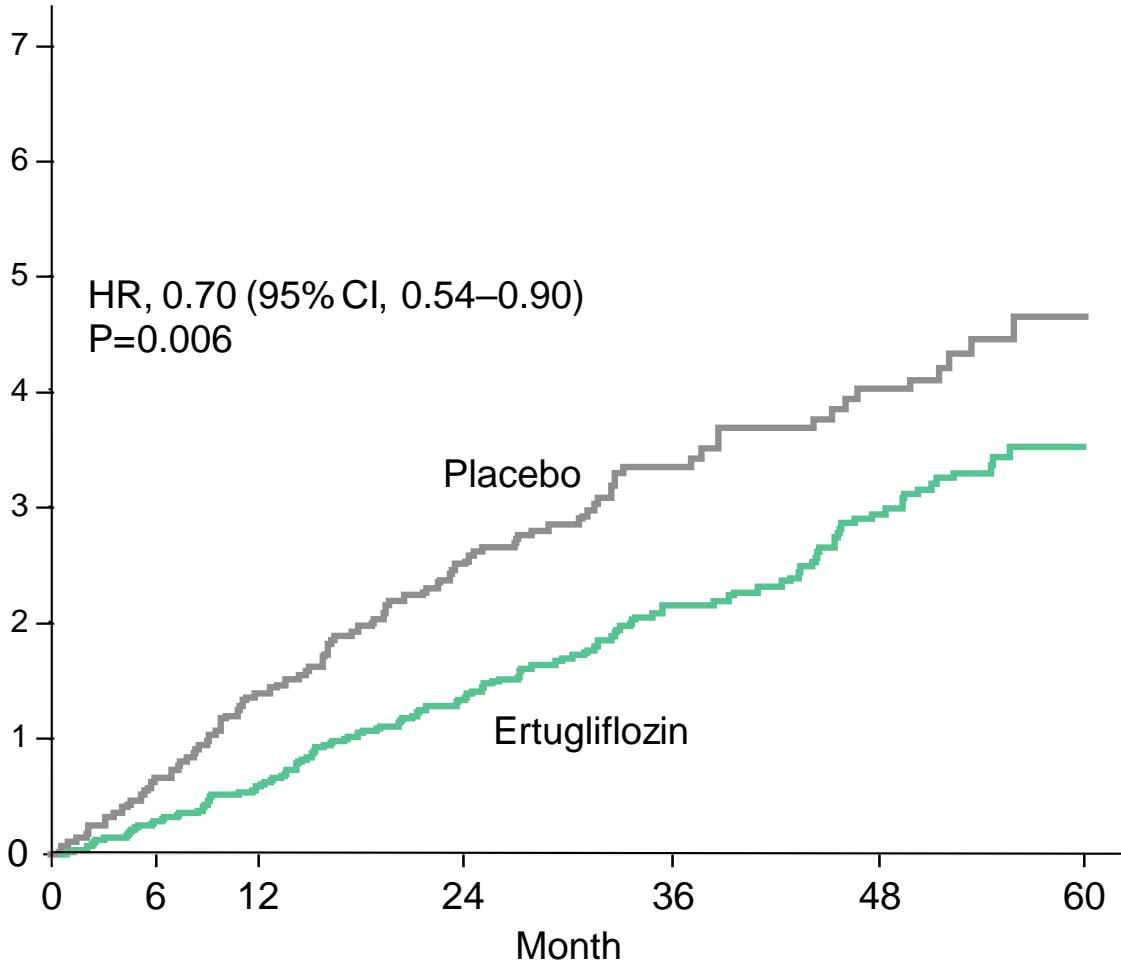


ASCVD, atherosclerotic cardiovascular disease; CI, confidence interval; MACE, major adverse cardiovascular events.

TIME TO FIRST HOSPITALISATION FOR HEART FAILURE



TIME TO FIRST HHF – SPOT THE DIFFERENCE?

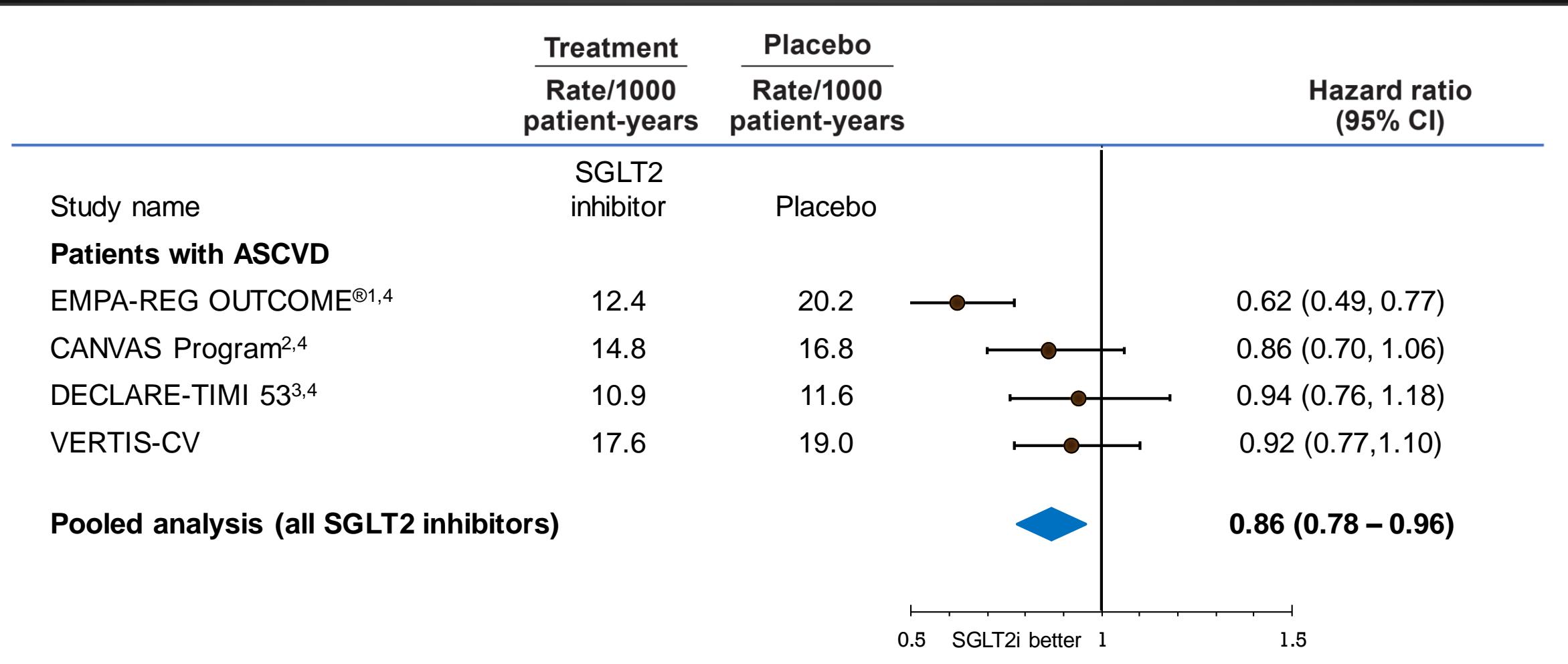


*Intention-to-treat analysis set that included all randomized patients with no upper limit on the ascertainment window for the superiority outcomes (N=5499 for ertugliflozin and N=2747 for placebo).
CI, confidence interval.; CV, cardiovascular; HFF, hospitalization for heart failure; HR, hazard ratio.

IS IT ALL JUST CLASS EFFECT?

- ✓ Chemical Structure
- ✓ Mechanism of Action
- ✓ HbA1c, Weight, BP
- ✓ CV Safety
- ✓ Reduced HHF
- ✓ Genital Mycoses, Ketoacidosis

TIME TO CV DEATH – IS THERE A DIFFERENCE?



IS THERE REALLY ANY DIFFERENCE?

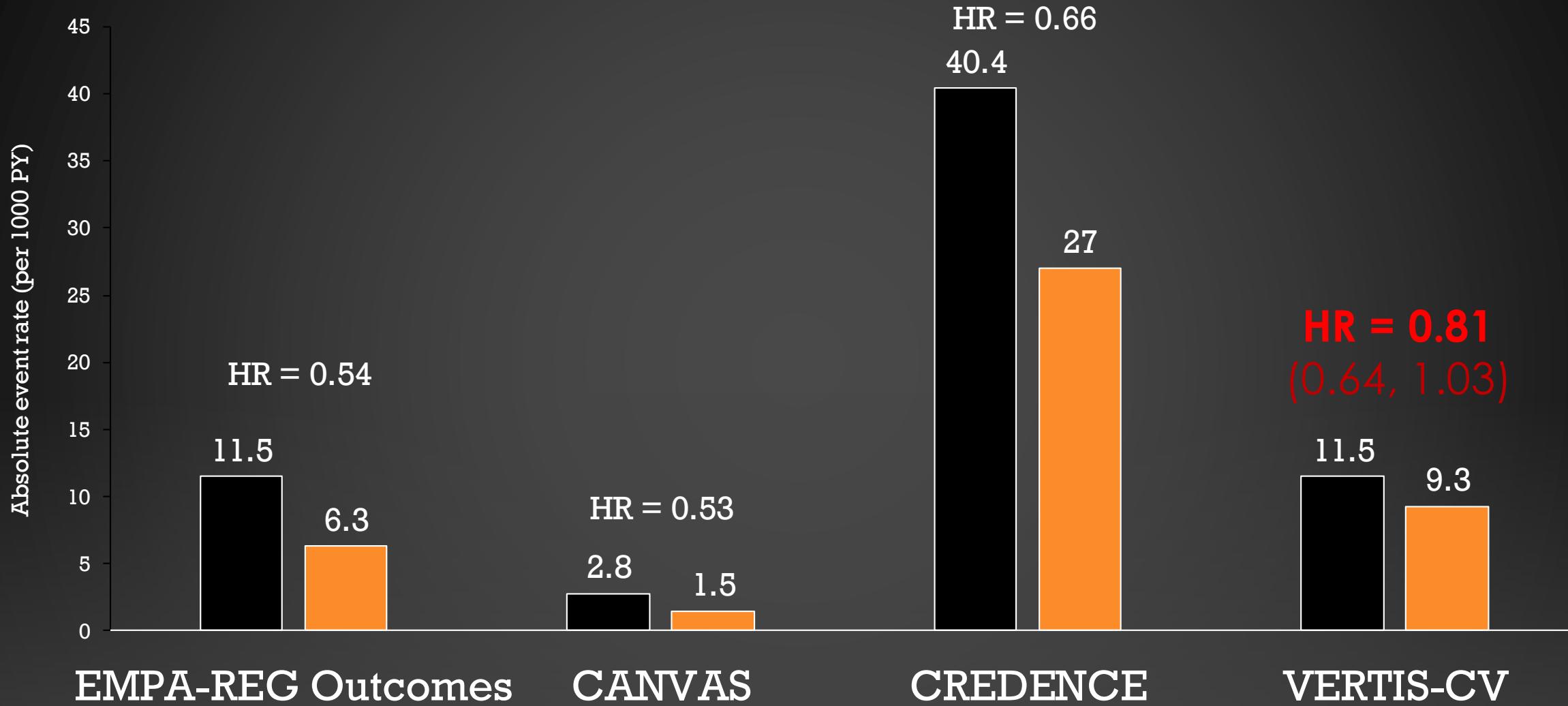
- Unlikely, based on so many similarities
- Not because of different baseline risk
- Not because of obvious trial/popⁿ differences
- Not a head to head comparison
- Random fluctuations around a mean?

IS IT ALL JUST CLASS EFFECT?

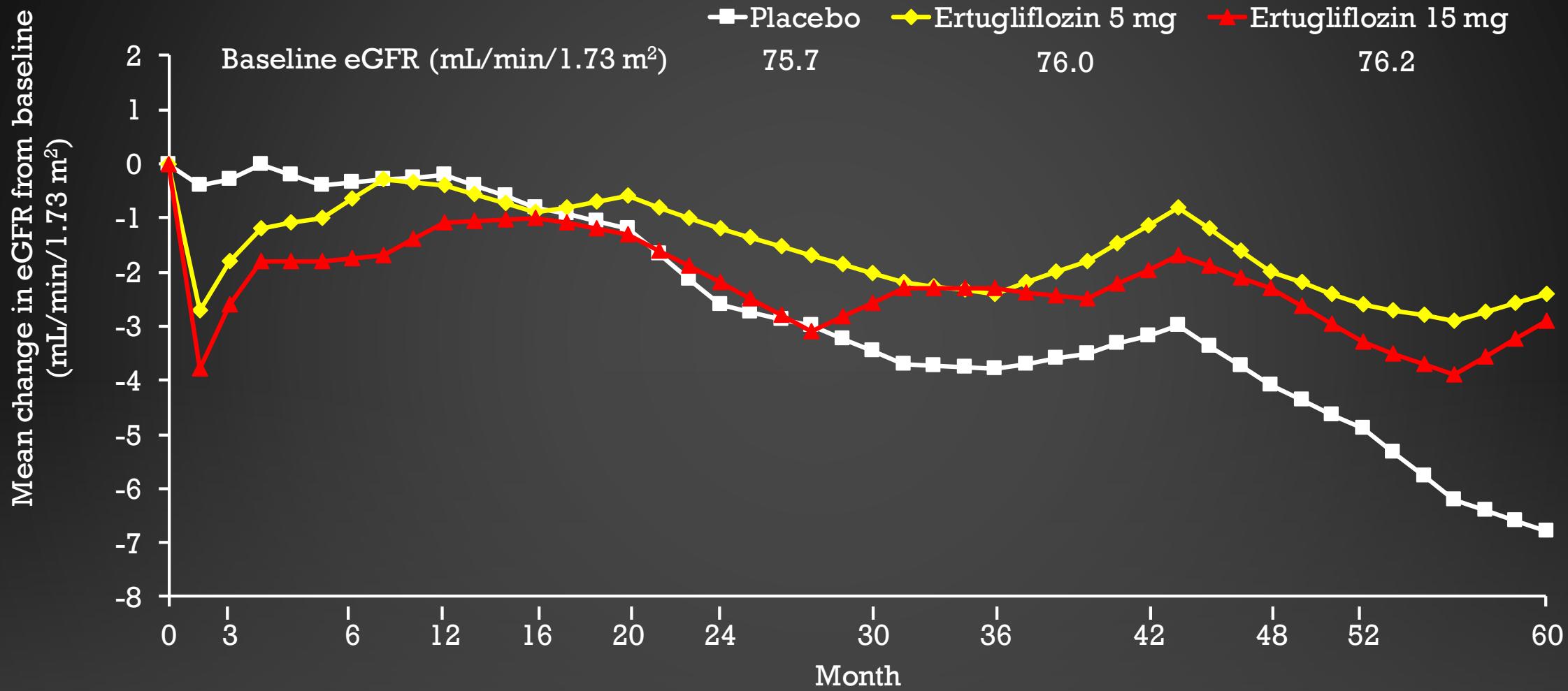
✓ Cardiovascular Death

Renal Protection?

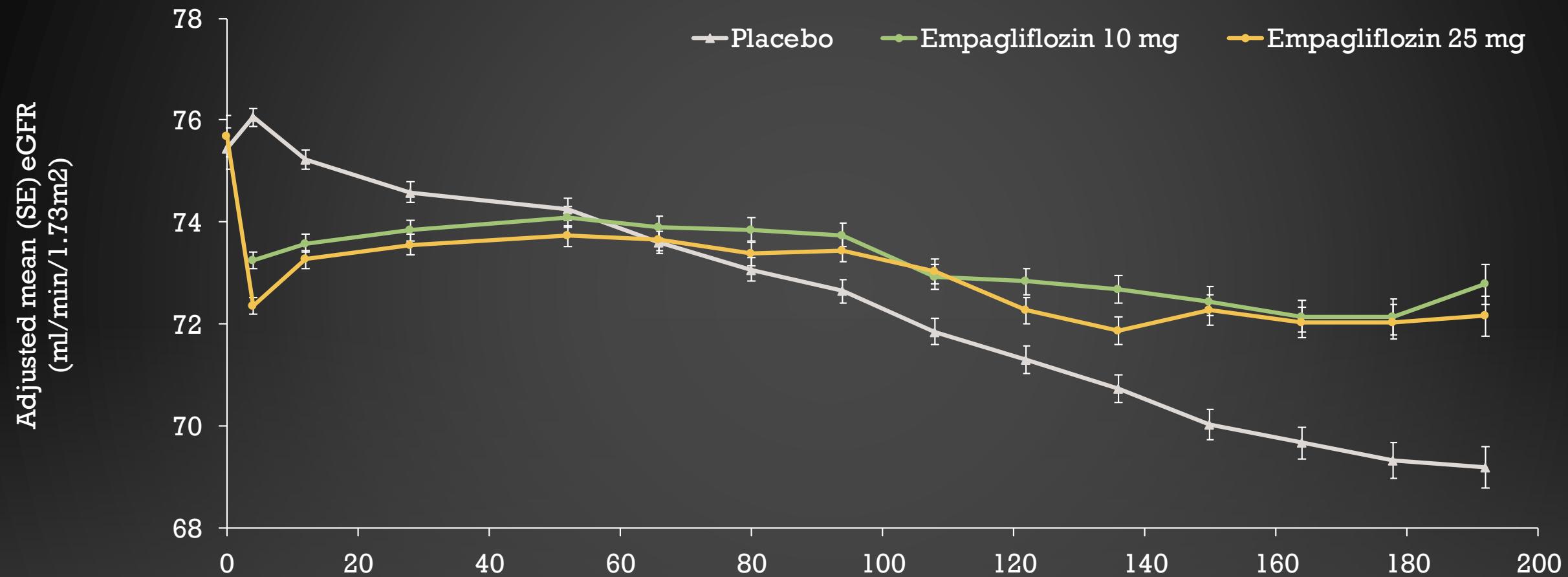
Doubling of serum creatinine, dialysis, transplantation or renal death



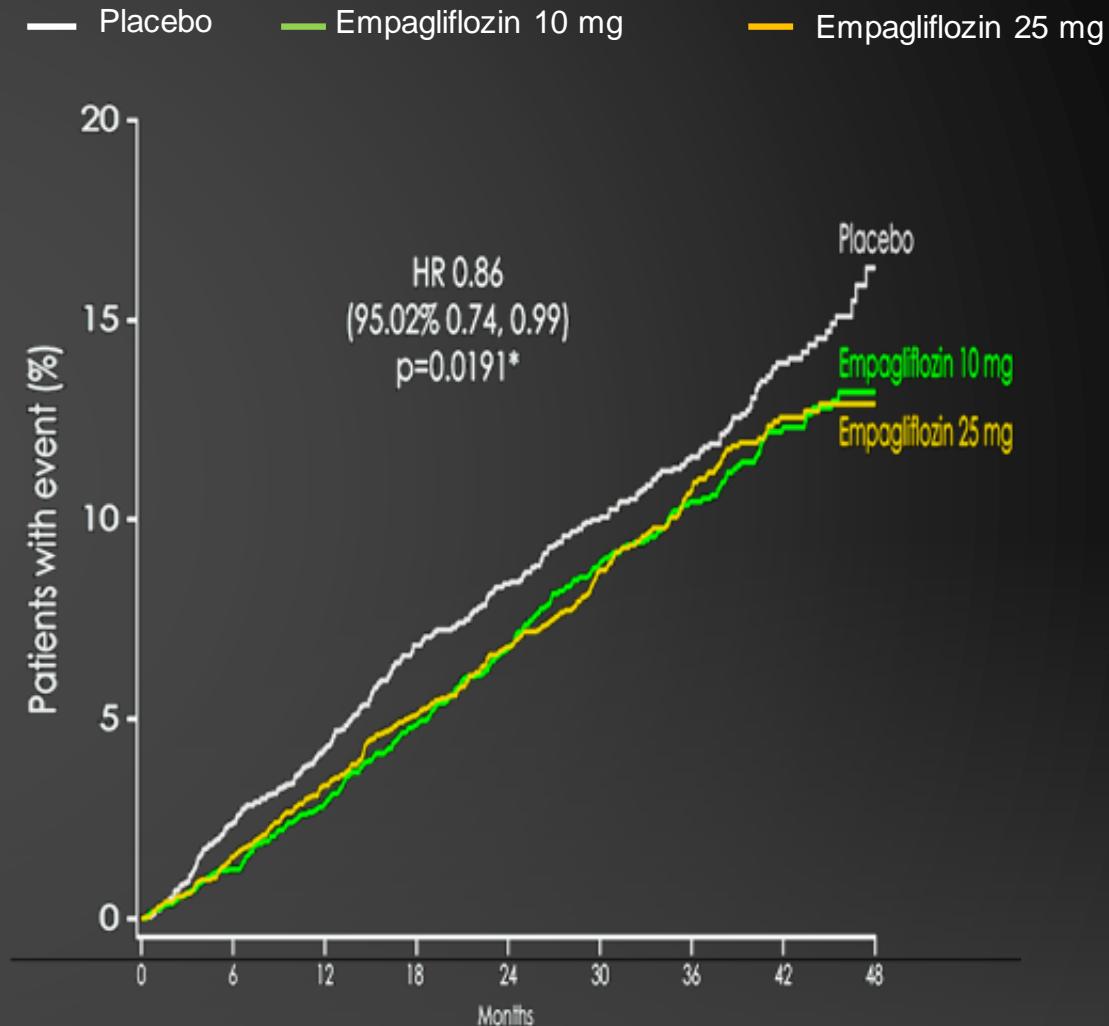
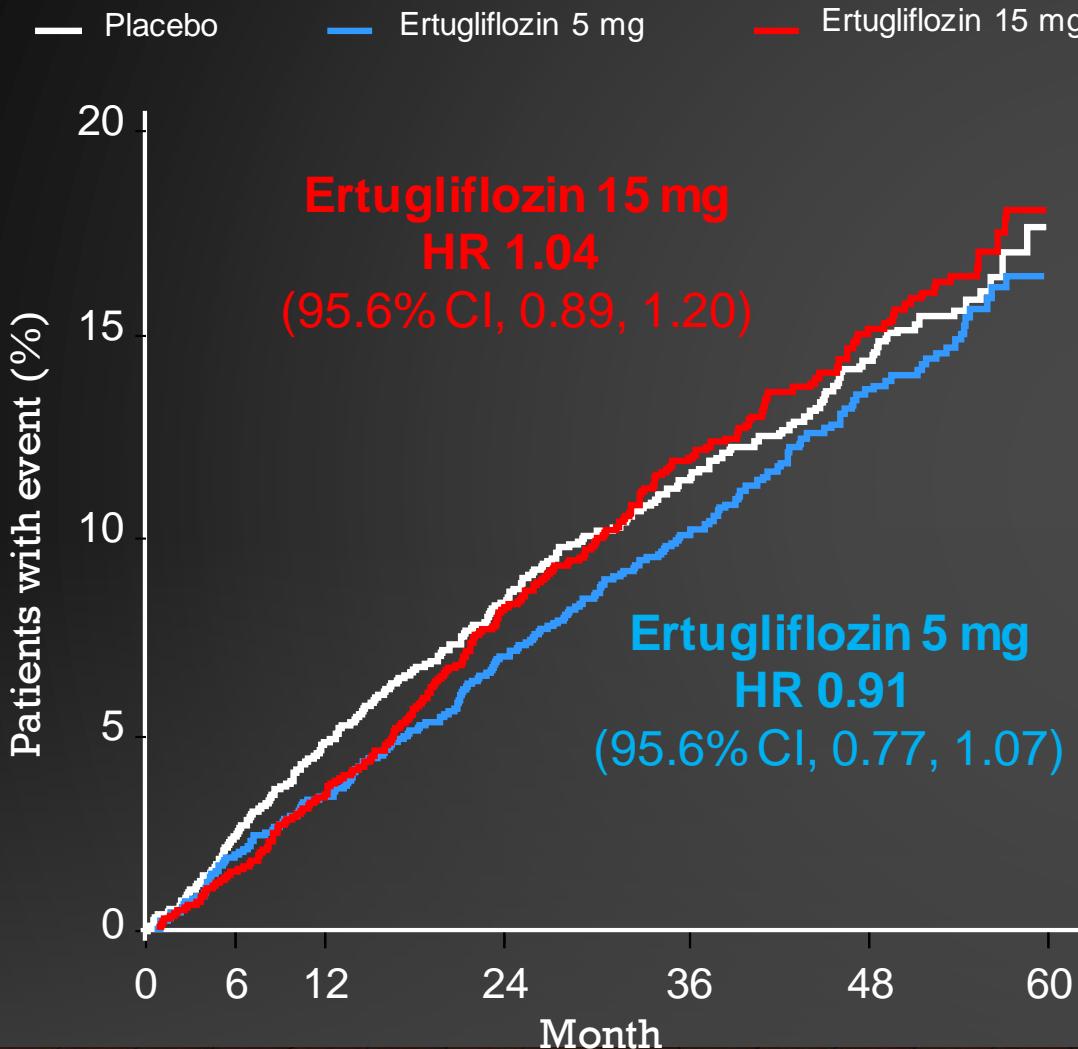
VERTIS-CV change in eGFR over time



EMPA-REG OUTCOMES change in eGFR over time



BUT WHAT HAPPENED TO THE DOSE?



VERTIS-CV – it's ^{probably} all class

Mark Cooper (ADA 2020)