SGLT2 INHIBITORS: CARDIOVASCULAR OUTCOMES TRIALS

	EMPA-REG OUTCOME 2016	CANVAS Program 2017	DECLARE-TIMI 58 2019	VERTIS CV 2020
DRUG	Empagliflozin 10-25 mg daily	Canagliflozin 100-300 mg daily	Dapagliflozin 10 mg daily	Ertugliflozin 5-15 mg daily
# RANDOMIZED	7020 (active, n=4687; placebo, n=2333)	10,141 (active, n=5764; placebo, n=4347)	17,160 (active, n=8582; placebo, n=8578)	8246 (active, n=5499; placebo, n=2747)
INCLUSION CRITERIA	• Type 2 diabetes; HgA1c 7.0-10% • Established cardiovascular disease • eGFR ≥30 mL/min	• Type 2 diabetes; HgA1c 7.0-10.5% • Established cardiovascular disease, or ≥2 risk factors • eGFR >30 mL/min	• Type 2 diabetes; HgA1c 6.5-12% • Established cardiovascular disease, or multiple risk factors • CrCl ≥60 mL/min	• Type 2 diabetes • HgA1c 7.0-10.5% • Established cardiovascular disease
BASELINE CHARACTERISTICS	• Age ~63 years; male ~71% • HgA1c ~8.1% • CAD ~76%; prior MI ~47%	• Age ~63 years; male ~64% • HgA1c ~8.2% • Established ASCVD ~72%	• Age ~64 years; male ~63% • HgA1c ~8.3% • Established ASCVD ~41%	• Age ~64 years; male ~70% • HgA1c ~8.2% • CAD ~76%
DURATION	Median follow-up period of 3.1 years	Median follow-up period of ~3.6 years	Median follow-up period of ~4.2 years	Mean follow-up period of 3.5 years
PRIMARY OUTCOME	Composite of cardiovascular death, non-fatal MI and non-fatal stroke	Composite of cardiovascular death, non-fatal MI and non-fatal stroke	Composite of cardiovascular death, myocardial infarction and stroke	Composite of cardiovascular death, non-fatal MI and non-fatal stroke
RESULTS	**Primary Composite Outcome:** 490 (10.5%) vs 282 (12.1%) HR 0.86 (95% CI 0.74-0.99) p=0.04; ARR 1.63%; NNT ~62	**Primary Composite Outcome:** 26.9 vs 31.5 (# pts per 1000 pt-years) HR 0.86 (95% CI 0.75-0.97); p=0.02	**Primary Composite Outcome:** NSD 756 (8.81%) vs 803 (9.36%); HR 0.93 (95% CI 0.84-1.03); p=0.17	**Primary Composite Outcome:** NSD 653/5493 (11.9%) vs 327/2745 (11.9%) HR 0.97 (95.6% CI 0.85-1.11)
MORBIDITY OUTCOMES	Non-Fatal MI: NSD Non-Fatal Stroke: NSD <u>Heart Failure Hospitalization:</u> 126 (2.69%) vs 95 (4.07%) HR 0.65 (95% CI 0.50-0.85) p=0.002; ARR 1.38%; NNT ~73	Non-Fatal MI: NSD Non-Fatal Stroke: NSD <u>Heart Failure Hospitalization:</u> 5.5 vs 8.7 (# pts per 1000 pt-years) HR 0.67 (95% CI 0.52-0.87)	Non-Fatal MI: NSD Non-Fatal Stroke: NSD <u>Heart Failure Hospitalization:</u> 212 (2.47%) vs 286 (3.33%) HR 0.73 (95% CI 0.61-0.88) ARR 0.86%; NNT ~116	Non-Fatal MI: NSD Non-Fatal Stroke: NSD <u>Heart Failure Hospitalization:</u> 139 (2.53%) vs 99 (3.60%) HR 0.70 (95% CI 0.54-0.90)
MORTALITY OUTCOMES	<u>Cardiovascular Death:</u> 172 (3.67%) vs 137 (5.87%) HR 0.62 (95% CI 0.49-0.77) p<0.001; ARR 2.20%; NNT ~46	<u>Cardiovascular Death:</u> NSD	<u>Cardiovascular Death:</u> NSD	<u>Cardiovascular Death:</u> NSD

These trials demonstrated the **cardiovascular safety** of SGLT2is in patients with type 2 diabetes. Additionally, there was consistent morbidity benefit demonstrate in the form of **reduced heart failure hospitalization** (which led to several subsequent landmark trials). Of these SGLT2is, only empagliflozin demonstrated **mortality benefit**. No SGLT2i demonstrated significantly reduced rates of non-fatal myocardial infarction or stroke.

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NSD: no significant difference