TABLE 1

Summary of patient characteristics and main cardiovascular outcomes

Better than usual care;
Worse than usual care

Trial [www.clinicaltrials.gov ID]	Trial dates	Follow-up (years)	Patient number	Patient baseline characteristics							Primary end-point	Primary end-point met by all studies	Non-fatal myocardial infarction	Non-fatal stroke	Hospitalisation for heart failure	CV death	All-cause death
				Age (years)	T2DM length (years)	HbA_{1c} % (mmol/mol)	Insulin ± GLD (%)	High BP (%)	Prior CV disease (%)	CV type		Hazard ratio and 95% confidence intervals					
TECOS[32] Sitagliptin [NCT00790205]	2008–2015	2.8	14,671	66	9.4	7.3 (56.3)	23	86	100	CVD	3 pt MACE and AngH	Yes HR: 0.98 CI: 0.89–1.08	HR: 0.95‡‡ CI: 0.81–1.11	HR: 0.97‡‡ CI: 0.89–1.08	HR: 1.00 CI: 0.83–1.20	HR: 1.03 CI: 0.89–1.19	HR: 1.01 CI: 0.90–1.14
EXAMINE[33] Alogliptin [NCT00968708]	2009–2014	1.5	5,400	61	7.2	8.0 (64.0)	30	83	100	ACS <90 days	3 pt MACE	Yes HR: 0.96 CI upper: ≤1.16	HR: 1.08 CI: 0.88–1.33	HR: 0.91 CI: 0.55–1.50	HR: 1.07 CI: 0.78–1.15	HR: 0.79 CI: 0.60–1.04	HR: 0.88 CI: 0.71–1.09
SAVOR[34] Saxagliptin [NCT01107886]	2010–2013	2.1	16,492	65	10	8.0 (64.0)	41	81	78	Age ≥40 years + CVD or ≥55 years + ≥1 CV risk factor	3 pt MACE	Yes HR: 1.0 CI: 0.89–1.08	HR: 0.95 CI: 0.80–1.12	HR: 1.11 CI: 0.88–1.39	HR: 1.27‡ CI: 1.07–1.51	HR: 1.03 CI: 0.87–1.22	HR: 1.11 CI: 0.96–1.27
EXSCEL[35] Exenatide weekly [NCT01144338]	2010–2017	3.2	14,752	63	12	8.0 (64.0)	46	73.1	73	CVD	3 pt MACE	Yes HR: 0.91 CI: 0.83–1.00	HR: 0.97‡‡ CI: 0.85–1.10	HR: 0.85‡‡ CI: 0.70–1.03	HR: 0.94 CI: 0.78–1.13	HR: 0.91 CI: 0.83–1.00	HR: 0.86 CI: 0.77–0.97
ELIXA[36] Lixisenatide [NCT01147250]	2010–2015	2.1	6,068	60	9.3	7.7 (60.7)	39	76.4	100	ACS <180 days	3 pt MACE and UA	Yes HR: 1.02 CI: 0.89–1.17	HR: 1.03‡‡ CI: 0.87–1.22	HR: 1.12‡‡ CI: 0.79–1.58	HR: 0.96 CI: 0.75–1.23	HR: 0.98 CI: 0.78–1.22	HR: 0.94 CI: 0.78–1.13
LEADER[37] Liraglutide [NCT01179048]	2010–2016	3.8	9,340	64.3	12.8	8.7 (71.6)	44	92	~81	Age ≥50 years + CVD (including heart failure) or CKD, or ≥60 years and ≥1 CV risk factor	3 pt MACE	Yes HR: 0.87‡ CI: 0.78–0.97	HR: 0.88 CI: 0.75–1.03	HR: 0.89 CI: 0.72–1.11	HR: 0.87 CI: 0.73–1.05	HR: 0.78‡ CI: 0.66–0.93	HR: 0.85‡ CI: 0.74–0.97
SUSTAIN 6[38] Semaglutide subcutaneous weekly [NCT01720446]	2013–2016	2.1	3,297	64.6	13.9	8.7 (71.6)	58	93	~83	Age ≥50 years + CVD (including heart failure) or CKD, or ≥60 years and ≥1 CV risk factor	3 pt MACE	Yes HR: 0.74‡ CI: 0.58–0.95	HR: 0.74 CI: 0.51–1.08	HR: 0.61‡ CI: 0.38–0.99	HR: 1.11 CI: 0.77–1.61	HR: 0.98 CI: 0.65–1.48	HR: 1.05 CI: 0.74–1.50
CANVAS[39] [NCT01032629] Canagliflozin (CANVAS-R† [NCT01989754])	2009–2017 2014–2017	3.1	10,142	63.3	13.5	8.2 (66.1)	50	90	65	Age ≥30 years + CVD, or ≥50 years + ≥2 CV risk factors	3 pt MACE	Yes HR: 0.86‡ CI: 0.75–0.97	HR: 0.85 CI: 0.69–1.05	HR: 0.90 CI: 0.71–1.15	HR: 0.67 CI: 0.52–0.87	HR: 0.87 CI: 0.72–1.06	HR: 0.87 CI: 0.74–1.01
EMPA-REG[40] (also known as C-SCADE 8) Empagliflozin [NCT01131676]	2010–2015	3.1	7,020	63	57% >10 years	8.1 (65)	48	94	99	CVD	3 pt MACE	Yes HR: 0.86‡ CI: 0.74–0.99	HR: 0.87 CI: 0.70–1.09	HR: 1.24 CI: 0.92–1.67	HR: 0.65‡ CI: 0.50–0.85	HR: 0.62‡ CI: 0.49–0.77	HR: 0.68‡ CI: 0.57–0.82
DEVOTE[41] Degludec vs glargine [NCT01959529]	2013–2017	1.99	7,637	65	16.4	7.5 (58.5)	100	94	85.2 (CVD/CKD)	Age ≥50 years + CVD/CKD, or ≥60 years + CV risk	3 pt MACE	Yes HR: 0.91 CI: 0.75–1.06	HR: 0.85 CI: 0.68–1.06	HR: 0.90 CI: 0.65–1.23	CI: 0.95‡‡‡ CI: 0.68–1.31	HR: 0.96 CI: 0.76–1.21	HR: 0.91 CI: 0.76–1.11

†CANVAS was originally designed for up to nine years, but amended to end when enough MACE events had accumulated between the CANVAS and CANVAS-R studies. Now referred to as the CANVAS Program.
‡ Statistically significant; ‡‡fatal and non-fatal; ‡‡‡ hospitalised for angina

ACS: acute coronary syndrome; Ang H: hospitalised for angina; CI: confidence interval; CV: cardiovascular; CVD: cardiovascular disease; CKD: chronic kidney disease; GLD: glucose-lowering drugs; HHF: hospitalised for heart failure; HR: hazard ratio; UA: urine albumin; 3pt MACE: Major adverse cardiac events (composite of cardiovascular death, non-fatal myocardial infarction and non-fatal stroke); T2DM: type 2 diabetes mellitus