

Supplementary Table 2. Definition of high risk of cardiovascular events in clinical trials

EMPA-REG trial (NEJM, 2015)
High risk of cardiovascular events defined as the presence of ≥ 1 of the following:
1) History of myocardial infarction >2 months prior to informed consent
2) Evidence of multi-vessel coronary artery disease (≥ 2) in major coronary arteries or the left main coronary artery, documented by any of the following: <ul style="list-style-type: none"> √ Presence of significant stenosis: $\geq 50\%$ luminal narrowing during angiography (coronary or multi-slice computed tomography) √ Previous revascularization (percutaneous transluminal coronary angioplasty \pm stent or coronary artery bypass graft) >2 months prior to consent √ Combination of revascularization in one major coronary artery and significant stenosis ($\geq 50\%$ luminal narrowing) in another major coronary artery
3) Evidence of single-vessel coronary artery disease $\geq 50\%$ luminal narrowing during angiography (coronary or multi-slice computed tomography) not subsequently successfully revascularized, with at least one of the following: <ul style="list-style-type: none"> √ A positive non-invasive stress test for ischemia √ Hospital discharge for unstable angina ≤ 12 months prior to consent
4) Unstable angina >2 months prior to consent with evidence of single- or multi-vessel coronary artery disease
5) History of stroke (ischemic or hemorrhagic) >2 months prior to consent
6) Occlusive peripheral artery disease documented by any of the following: <ul style="list-style-type: none"> √ Limb angioplasty, stenting, or bypass surgery √ Limb or foot amputation due to circulatory insufficiency √ Evidence of significant peripheral artery stenosis (>50% on angiography, or >50% or hemodynamically significant via non-invasive methods) in one limb √ Ankle brachial index <0.9 in ≥ 1 ankle
DECLARE-TIMI 58 trial (NEJM, 2019)
High risk for CV event defined as having either established CV disease and/or multiple risk factors:
Established CV disease, defined as any of the following:
1) Ischemic heart disease (any of the following): <ul style="list-style-type: none"> √ Documented myocardial infarction √ Percutaneous coronary intervention or coronary artery bypass grafting √ Objective findings of coronary stenosis ($\geq 50\%$) in at least two coronary artery territories (such as, left anterior descending, ramus intermedius, left circumflex, and right coronary artery) involving the main vessel, a major branch, or a bypass graft
2) Cerebrovascular disease (any of the following): <ul style="list-style-type: none"> √ Documented ischemic stroke (known transient ischemic attack, primary intracerebral hemorrhage, or sub-arachnoid hemorrhage do not qualify) √ Carotid stenting or endarterectomy
3) Peripheral arterial disease (any of the following): <ul style="list-style-type: none"> √ Peripheral arterial intervention, stenting, or surgical revascularization √ Lower extremity amputation as a result of peripheral arterial obstructive disease √ Current symptoms of intermittent claudication AND ankle/brachial index (ABI) <0.90 documented within the last 12 months
OR no known cardiovascular disease AND at least two cardiovascular risk factors in addition to T2DM, defined as:
1) Age ≥ 55 years in men and ≥ 60 in women AND
2) Presence of at least one of the following additional risk factors <ul style="list-style-type: none"> √ Dyslipidemia (at least one of the following) <ul style="list-style-type: none"> - LDL-C > 130 mg/dL (3.36 mmol/L) within the last 12 months - On a lipid lowering therapy prescribed by a physician for hypercholesterolemia (that is, LDL-C > 130 mg/dL (3.36 mmol/L) for greater than 12 months. This should be verified by documentation of lab value LDL-C > 130 mg/dL (3.36 mmol/L). √ Hypertension (at least one of the following) <ul style="list-style-type: none"> - BP > 140/90 mm Hg at enrollment. The patient must have both an elevated systolic BP (> 140 mm Hg) and an elevated diastolic BP (> 90 mm Hg) on both measurements. - On an anti-hypertensive therapy prescribed by a physician for lowering the blood pressure √ Current tobacco use (5 cigarettes/day or more for at least 1 year at randomization)

EMPA-REG, the Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes; NEJM, *New England Journal of Medicine*; DECLARE-TIMI, The Dapagliflozin Effect on Cardiovascular Events; CV, cardiovascular; T2DM, type 2 diabetes mellitus; LDL-C, low-density lipoprotein cholesterol; BP, blood pressure.