

Table 1. Population, Intervention, Comparator and Outcomes for evaluating the comparative efficacy and safety of glucose-lowering medications as add-on therapy to metformin for diabetics with or without a known history of heart failure

	Inclusion	Exclusion
Population	Adults with type 2 diabetes with or without known heart failure who cannot attain adequate glucose control with metformin, or for whom metformin cannot be used	Type 1 diabetes; Adults not on metformin or without contraindication or intolerance for metformin; Adults on metformin plus a second glucose-lowering medication
Interventions	GLP-1 (receptor) agonists SGLT-2 inhibitors	Alpha-glucosidase inhibitors; Meglitinides
Comparator	Placebo	Alpha-glucosidase inhibitors; Meglitinides
Outcomes	Heart failure events Hospitalization for heart failure All-cause death	Cardiovascular death Composite outcomes of death from CV causes, nonfatal MI or nonfatal stroke (MACE)

Table 2. Population, Intervention, Comparator and Outcomes for evaluating the efficacy and safety of glucose-lowering medications as add-on therapy to metformin for diabetics with or without a known history of chronic kidney disease, microalbuminuria or macroalbuminuria

	Inclusion	Exclusion
Population	Adults with type 2 diabetes with or without chronic kidney disease who cannot attain adequate glucose control with metformin, or for whom metformin cannot be used	Type 1 diabetes; Adults not on metformin or without contraindication or intolerance for metformin; Adults on metformin plus a second glucose-lowering medication
Interventions	GLP-1 (receptor) agonists SGLT-2 inhibitors	Alpha-glucosidase inhibitors Meglitinides
Comparator	Placebo	Alpha-glucosidase inhibitors Meglitinides
Outcomes	Pre-specified composite renal outcome incorporating change in serum creatinine level, eGFR reduction, initiation of renal-replacement therapy or death from renal disease Acute kidney injury Acute renal failure Death due to renal causes ESRD All-cause death	Composite outcomes of death from CV causes, nonfatal MI or nonfatal stroke (MACE) New or worsening nephropathy Nephropathy Progression of albuminuria