# Table 2. Outcome for patients with type 2 diabetes and established cardiovascular disease

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| **Study** | **Class of drug** | **Drug** | **Median follow-up, yrs** | **Reduction of (NNT)** | | | **Specific adverse effects (NNH1)** | **Evidence for benefit/harm of investigational drug** |
| **Primary composite cardiovascular endpoint** | **Secondary cardiovascular endpoints** | **All-cause mortality** |
| EMPA-REG OUTCOME | SGLT2 inhibitor | Empagliflozin | 3.1 | yes (61) | cardiovascular death (45),  heart failure hospitalization (72) | yes (39) | genital infection (22),  volume depletion in patients > 75 years, ketoacidosis | **relevant benefit, particularly for patients at risk or with HF** |
| CANVAS1 Program | Canagliflozin | 2.4 | yes (72) | heart failure hospitalization (1041, exploratory analysis) | no | amputation (1151),  low-trauma fractures,  male genitalia infection (141) | **relevant benefit at the cost of increased risk of amputations** |
| LEADER | GLP-1 receptor agonist | Liraglutide | 3.8 | yes (55) | cardiovascular death (79) | yes (71) | injection site reaction with once daily sc injection (233),  drug discontinuation due to nausea (79),  acute gallstone disease (85) | **relevant benefit** |
| SUSTAIN-6 | Semaglutide | 2.1 | yes (43) | non-fatal stroke (97) | no | retinopathy (78)  gastrointestinal disorders (66) | **relevant benefit** |
| EXSCEL | Exenatide | 3.2 | no | no | no (exploratory analysis yes (100)) | thyroid papillary carcinomas  (n =10 vs. 4) | **non-significant trend for benefit** |
| ELIXA | Lixisenatide | 2.1 | no | no | No | gastrointestinal disorders leading to drug discontinuation (27) | **no benefit** |
| PROACTIVE | thiazolidinedione | Pioglizatone | 2.9 | no | composite endpoint of all-cause mortality, non-fatal MI and stroke (49),  increase of HF hospitalization (NNH=62) | No | oedema wo heart failure (12) | **potential benefit, increased risk of HF hospitalization** |
| SAVOR-TIMI 53 | dipeptidyl peptidase 4 inhibitor | Saxagliptin | 2.1 | no | increase of HF hospitalization (NNH=140) | No | increased (but very rare) occurrence of non-fatal angioedema | **no benefit, increased risk of HF hospitalization** |
| EXAMINE | Alogliptin | 2.1 | no | no | No | NR | **no benefit** |
| TECOS | Sitagliptin | 3.0 | no | no | No | NR | **no benefit** |
| UKPDS 34 | biguanide | Metformin | 10.7 | yes (11) | non-fatal MI (16) | yes (11) | NR | **potential cardiovascular benefit in patients wo CVD** |
| STOP-NIDDM | alpha-glucosidase inhibitor | Acarbose (compared to sulfonylurea) | 3.38 | yes (40) | non-fatal MI (62) | NR | premature study drug discontinuation (8) | **hypothesis generation for potential cardiovascular benefit in patients wo CVD** |

NNT/NNH number needed to treat/harm was calculated only for significant results with the formula 100/absolute difference of endpoint in % for the given follow-up period, NR not reported, ACS acute coronary syndrome, 1) NNTs/NNHs were calculated based on the given event rates per 1000 patient years and transformed for a follow-up of 3 years;