**Table D7. Results of studies evaluating effects of diabetes medications on long-term clinical outcomes**

| **Author, year**  **Study design** | **Intervention** | **Overall mortality, n (%)** | **CVD mortality, n (%)** | **CVD morbidity, n (%)** | **Cerebrovascular disease, n (%)** |
| --- | --- | --- | --- | --- | --- |
| Ahren, 2014[2](#_ENREF_2) | Grp1: Metformin + placebo  Fixed >=1500 mg  Grp2: Metformin + glimepiride + placebo  Fixed >=1500 mg  Titrated 2 mg qdup-titration to 4mg qd | Def: All-cause mortality  Incidence Grp1: 1  Incidence Gp2: 3 |  |  |  |
| Ahren, 2014[2](#_ENREF_2) | Grp1: Metformin + placebo  Fixed >=1500 mg  Grp2: Metformin + sitagliptin + placebo  Fixed >=1500 mg  Fixed 100 mg qd | Def: All-cause mortality  Incidence Grp1: 1  Incidence Grp2: 1 |  |  |  |
| Ahren, 2014[2](#_ENREF_2) | Grp1: Metformin + placebo  Fixed >=1500 mg  Grp2: Metformin + albiglutide + placebo  Fixed >=1500 mg  Titrated 30 mg qwup-titration to 50 mg qw | Def: All-cause mortality  Incidence Grp1: 1  Incidence Grp2: 3 |  |  |  |
| Alba, 2013[3](#_ENREF_3)  RCT | Grp1: Pioglitazone Fixed (30mg) Grp2: Sitagliptin Fixed (100mg) ITT: Yes Followup (wks): 52  NR/unclear | Def:All-cause mortality Incidence Grp1: 0   Persons p NR  Incidence Grp2: 0   Persons p NR |  |  |  |
| Andersson, 2010[190](#_ENREF_190)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 52  NR/unclear | Def:All-cause mortality Incidence Grp1: 0   Persons p NR  Incidence Grp2: 0   Persons p NR |  |  |  |
| Andersson, 2010[190](#_ENREF_190)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 26 | Def:All-cause mortality Incidence Grp1: 0  177 Persons p NR  Incidence Grp2: 0  315 Persons p NR |  |  |  |
| Andersson, 2010[190](#_ENREF_190)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Metformin + su Not specified   Not specified   ITT: Yes Followup (wks): 52 | Def:All-cause mortality Incidence Grp1:   Persons p NR  Incidence Grp2: 2  315 Persons p NR |  |  |  |
| Andersson, 2010[190](#_ENREF_190)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Metformin + su Not specified   Not specified   ITT: Yes Followup (wks): 26 | Def:All-cause mortality Incidence Grp1: 0  177 Persons p NR  Incidence Grp2: 0  302 Persons p NR |  |  |  |
| Andersson, 2010[190](#_ENREF_190)  Retrospective cohort | Grp1: SU Not specified   Grp2: Metformin + su Not specified   Not specified   ITT: Yes Followup (wks): 52 | Def:All-cause mortality Incidence Grp1:   Persons p NR  Incidence Grp2: 0  302 Persons p NR |  |  |  |
| Andersson, 2010[190](#_ENREF_190)  Retrospective cohort | Grp1: SU Not specified   Grp2: Metformin + su Not specified   Not specified   ITT: Yes Followup (wks): 52 | Def:All-cause mortality Incidence Grp1:   Persons p NR  Incidence Grp2: 1  304 Persons p NR |  |  |  |
| Arechavaleta, 2011[5](#_ENREF_5)  RCT | Grp1: Metformin + glimepiride + placebo Not specified (on stable metformin >=1500 mg at screening for the past 12 wks) Titrated (Median: 2.1mg/day after wk 18 (at end of titration period)Max: 6mg/day) Grp2: Metformin + sitagliptin + placebo Not specified (on at least 1500 mg daily for 12 wks prior to screening at stable dose) Fixed (100mg daily) ITT: Yes Followup (wks): 26 | Def:All-cause mortality Incidence Grp1: 0  177 Persons p NR  Incidence Grp2: 1  304 Persons p NR |  |  |  |
| Arechavaleta, 2011[5](#_ENREF_5)  RCT | Grp1: Metformin + glimepiride + placebo Not specified (on stable metformin >=1500 mg at screening for the past 12 wks) Titrated (Median: 2.1mg/day after wk 18 (at end of titration period)Max: 6mg/day) Grp2: Metformin + sitagliptin + placebo Not specified (on at least 1500 mg daily for 12 wks prior to screening at stable dose) Fixed (100mg daily) ITT: Yes Followup (wks): 26 | Def:All-cause mortality  Incidence Grp1: 0  315 Persons p NR  Incidence Grp2: 0  302 Persons p NR |  |  |  |
| Arjona Ferreira, 2013[6](#_ENREF_6)  RCT | Grp1: Glipizide + placebo Titrated (Mean: 7.7mgMax: 20mg as considered appropriate by the investigator based on the pateint's glycemic controlstarting dose of 2.5mg, the dose could also be reduced or interrupted to prevent hypoglycemia) Grp2: Sitagliptin + placebo Fixed (50mg for pateitns with moderate renal insufficiency, 25mg for patients with severe renal insufficiency, dose was reduced from 50 to 25mg for patients whose renal status changed from moderate to severe during the study)    ITT: Yes Followup (wks): 52 | Def:All-cause mortality Incidence Grp1: 2  315 Persons p NR  Incidence Grp2: 0  302 Persons p NR |  |  |  |
| Arjona Ferreira, 2013[6](#_ENREF_6)  RCT | Grp1: Glipizide + placebo Titrated (Mean: 7.7mgMax: 20mg as considered appropriate by the investigator based on the pateint's glycemic controlstarting dose of 2.5mg, the dose could also be reduced or interrupted to prevent hypoglycemia) Grp2: Sitagliptin + placebo Fixed (50mg for pateitns with moderate renal insufficiency, 25mg for patients with severe renal insufficiency, dose was reduced from 50 to 25mg for patients whose renal status changed from moderate to severe during the study) ITT: Yes Followup (wks): 52 | Def:All-cause mortality Incidence Grp1: 2  315 Persons p NR  Incidence Grp2: 1  304 Persons p NR |  |  |  |
| Arjona Ferreira, 2013[6](#_ENREF_6)  RCT | Grp1: Glipizide + placebo Titrated (Mean: 7.7mgMax: 20mg as considered appropriate by the investigator based on the pateint's glycemic controlstarting dose of 2.5mg, the dose could also be reduced or interrupted to prevent hypoglycemia) Grp2: Sitagliptin + placebo Fixed (50mg for pateitns with moderate renal insufficiency, 25mg for patients with severe renal insufficiency, dose was reduced from 50 to 25mg for patients whose renal status changed from moderate to severe during the study) ITT: Yes Followup (wks): 26 | Def:All-cause mortality Incidence Grp1: 0  315 Persons p NR  Incidence Grp2: 1  304 Persons p NR |  |  |  |
| Arjona Ferreira, 2013[6](#_ENREF_6)  RCT | Grp1: Glipizide + placebo Titrated (Mean: 7.7mgMax: 20mg as considered appropriate by the investigator based on the pateint's glycemic controlstarting dose of 2.5mg, the dose could also be reduced or interrupted to prevent hypoglycemia) Grp2: Sitagliptin + placebo Fixed (50mg for pateitns with moderate renal insufficiency, 25mg for patients with severe renal insufficiency, dose was reduced from 50 to 25mg for patients whose renal status changed from moderate to severe during the study) ITT: No Followup (wks): 26  Active | Def:All-cause mortality Incidence Grp1: 0   NA p  Incidence Grp2: 0   NA p |  |  |  |
| Arjona Ferreira, 2013[6](#_ENREF_6)  RCT | Grp1: Glipizide + placebo Titrated (Mean: 7.7mgMax: 20mg as considered appropriate by the investigator based on the pateint's glycemic controlstarting dose of 2.5mg, the dose could also be reduced or interrupted to prevent hypoglycemia) Grp2: Sitagliptin + placebo Fixed (50mg for pateitns with moderate renal insufficiency, 25mg for patients with severe renal insufficiency, dose was reduced from 50 to 25mg for patients whose renal status changed from moderate to severe during the study) ITT: No Followup (wks): 26  Active | Def:All-cause mortality  Incidence Grp1: 0   NA p  Incidence Grp2: 0   NA p |  |  |  |
| Arjona Ferreira, 2013[6](#_ENREF_6)  RCT | Grp1: Glipizide + placebo Titrated (Mean: 7.7mgMax: 20mg as considered appropriate by the investigator based on the pateint's glycemic controlstarting dose of 2.5mg, the dose could also be reduced or interrupted to prevent hypoglycemia) Grp2: Sitagliptin + placebo Fixed (50mg for pateitns with moderate renal insufficiency, 25mg for patients with severe renal insufficiency, dose was reduced from 50 to 25mg for patients whose renal status changed from moderate to severe during the study) ITT: No Followup (wks): 26  Active | Def:All-cause mortality Incidence Grp1: 0   NA p  Incidence Grp2: 0   NA p |  |  |  |
| Aschner, 2010[7](#_ENREF_7)  RCT | Grp1: Metformin  Varied, prespecified target dose  Start: 500 mg, Max: 2000 mg, Mean: 1903  D: 5 wks  Grp2: Sitagliptin  Fixed  Mean: 100 mg | Grp1: 0 (0)  Grp2: 1 (<1) |  |  |  |
| Aschner, 2012[8](#_ENREF_8)  RCT | Grp1: Metformin + sitagliptin Not specified (baseline dose of metformin was 1835 mg) Fixed (100 mg) Grp2: Metformin + insulin glargine Not specified (mean baseline dose 1852 mg) Titrated (0.5 U/kg at 24 wks) ITT: No Followup (wks): 26  Active | Def:All-cause mortality Incidence Grp1: 0   NA p  Incidence Grp2: 0   NA p |  |  |  |
| Aschner, 2012[8](#_ENREF_8)  RCT | Grp1: Metformin + sitagliptin Not specified (baseline dose of metformin was 1835 mg) Fixed (100 mg) Grp2: Metformin + insulin glargine Not specified (mean baseline dose 1852 mg) Titrated (0.5 U/kg at 24 wks) ITT: No Followup (wks): 26  Active | Def:All-cause mortality Incidence Grp1: 0   NA p  Incidence Grp2: 0   NA p |  |  |  |
| Aschner, 2012[8](#_ENREF_8)  RCT | Grp1: Metformin + sitagliptin Not specified (baseline dose of metformin was 1835 mg) Fixed (100 mg) Grp2: Metformin + insulin glargine Not specified (mean baseline dose 1852 mg) Titrated (0.5 U/kg at 24 wks) ITT: No Followup (wks): 26  Active | Def:All-cause mortality Incidence Grp1: 0   NA p  Incidence Grp2: 0   NA p |  |  |  |
| Aschner, 2012[8](#_ENREF_8)  RCT | Grp1: Metformin + sitagliptin Not specified (baseline dose of metformin was 1835 mg) Fixed (100 mg) Grp2: Metformin + insulin glargine Not specified (mean baseline dose 1852 mg) Titrated (0.5 U/kg at 24 wks) ITT: No Followup (wks): 26  Active | Def:All-cause mortality Incidence Grp1: 0   NA p  Incidence Grp2: 0   NA p |  |  |  |
| Bailey, 2005[9](#_ENREF_9)  RCT | Grp1: Metformin  Varied  Start: 2500 mg, Max: 3000 mg  Grp2: Metformin + rosiglitazone  Fixed; Varied  Start: 2500mg; Start: 4 mg, Max: 8 mg | Grp1: 0 (0)  Grp2: 1 (<1) | Def: CVD mortality/sudden cardiac death  Grp1: 0 (0)  Grp2: 1 (<1) | Def: CVD morbidity/MI (non-fatal) + pulmonary edema with MI  Grp1: 0 (0)  Grp2: 1 (<1) |  |
| Bailey, 2013[10](#_ENREF_10)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1861 mgMedian: 1500 mg) Grp2: Metformin + dapagliflozin + placebo Fixed (Mean: 1792 mgMedian: 1500 mg) Fixed (2.5 mg) ITT: No Followup (wks): 26  Active | Def:All-cause mortality Incidence Grp1: 0   NA p  Incidence Grp2: 0   NA p |  |  |  |
| Bailey, 2013[10](#_ENREF_10)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1861 mgMedian: 1500 mg) Grp2: Metformin + dapagliflozin Fixed (Mean: 1854 mgMedian: 2000 mg) Fixed (5.0 mg) ITT: Yes Followup (wks): 52  Passive | Def:All-cause mortality Incidence Grp1: 1    Incidence Grp2: 2 |  |  |  |
| Bailey, 2013[10](#_ENREF_10)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1861 mgMedian: 1500 mg) Grp2: Metformin + dapagliflozin + placebo Fixed (Mean: 1800 mgMedian: 1500 mg) Fixed (10.0 mg) ITT: Yes Followup (wks): 52  Passive | Def:All-cause mortality  Incidence Grp1: 1    Incidence Grp2: 1 |  |  |  |
| Bailey, 2013[10](#_ENREF_10)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1861 mgMedian: 1500 mg) Grp2: Metformin + dapagliflozin + placebo Fixed (Mean: 1792 mgMedian: 1500 mg) Fixed (2.5 mg) ITT: No Followup (wks): 26  Active | Def:All-cause mortality Incidence Grp1: 1 (0.6) NR p NR  Incidence Grp2: 0 (0) NR p NR |  |  |  |
| Bailey, 2013[10](#_ENREF_10)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1861 mgMedian: 1500 mg) Grp2: Metformin + dapagliflozin Fixed (Mean: 1854 mgMedian: 2000 mg) Fixed (5.0 mg) ITT: No Followup (wks): 26  Active | Def:All-cause mortality Incidence Grp1: 1 (0.6) NR p NR  Incidence Grp2: 0 (0) NR p NR |  |  |  |
| Bailey, 2013[10](#_ENREF_10)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1861 mgMedian: 1500 mg) Grp2: Metformin + dapagliflozin + placebo Fixed (Mean: 1800 mgMedian: 1500 mg) Fixed (10.0 mg) ITT: Yes Followup (wks): 52  Passive | Def:All-cause mortality Incidence Grp1:   Persons p NR  Incidence Grp2: 1 (0.3) Persons p NR |  |  |  |
| Bailey, 2013[10](#_ENREF_10)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1861 mgMedian: 1500 mg) Grp2: Metformin + dapagliflozin + placebo Fixed (Mean: 1792 mgMedian: 1500 mg) Fixed (2.5 mg) ITT: Yes Followup (wks): 52  Passive | Def:All-cause mortality Incidence Grp1:   Persons p NR  Incidence Grp2: 0 (0) Persons p NR |  |  |  |
| Bailey, 2013[10](#_ENREF_10)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1861 mgMedian: 1500 mg) Grp2: Metformin + dapagliflozin Fixed (Mean: 1854 mgMedian: 2000 mg) Fixed (5.0 mg) ITT: Yes Followup (wks): 52  Passive | Def:All-cause mortality Incidence Grp1:   Persons p NR  Incidence Grp2: 1 (0.3) Persons p NR |  |  |  |
| Bailey, 2013[10](#_ENREF_10)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1861 mgMedian: 1500 mg) Grp2: Metformin + dapagliflozin + placebo Fixed (Mean: 1800 mgMedian: 1500 mg) Fixed (10.0 mg) ITT: Yes Followup (wks): 52  Passive | Def:All-cause mortality Incidence Grp1: 1 (0.3) Persons p NR  Incidence Grp2: 0 (0) Persons p NR |  |  |  |
| Bakris, 2006[12](#_ENREF_12)  RCT | Grp1: Metformin + rosiglitazone  Varied, NS; Varied, glucose: ≤ 6.6 mmol/L  Unclear; Start: 4mg  D: 3 wks  Grp2: Metformin + glyburide  Varied, NS; Varied, glucose: ≤ 6.6mmol/L  Unclear; Start: 5 mg  D: 3 wks | Grp1: 1 (1)  Grp2: 0 (0) |  |  |  |
| Barnett, 2012[13](#_ENREF_13)  RCT | Grp1: Glimepiride Titrated (Max: 4mg qdplacebo for 1st 18 wks then only for 19-52 wks, initiated at 1mg qd and uptitrated in 1mg increments every 4 wks to 4mg qd max if fassting blood glucose was >110mg/dl (6.1mmol/l)) Grp2: Linagliptin Fixed (5mg qdstarted this at randomization and on for all 52 wks) ITT: Yes Followup (wks): 52  Passive | Def:All-cause mortality Incidence Grp1: 1 (0.3) Persons p NR  Incidence Grp2: 1 (0.3) Persons p NR |  |  |  |
| Barnett, 2012[13](#_ENREF_13)  RCT | Grp1: Glimepiride Titrated (Max: 4mg qdplacebo for 1st 18 wks then only for 19-52 wks, initiated at 1mg qd and uptitrated in 1mg increments every 4 wks to 4mg qd max if fassting blood glucose was >110mg/dl (6.1mmol/l)) Grp2: Linagliptin Fixed (5mg qdstarted this at randomization and on for all 52 wks) ITT: No Followup (wks): 52  NR/unclear | Def:All-cause mortality Incidence Grp1: 2    Incidence Grp2: 0 |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1480mg) Fixed (45mg daily) Grp2: Metformin + sitagliptin + placebo Fixed (Mean: 1583mg) Fixed (100mg daily) ITT: No Followup (wks): 52  NR/unclear | Def:All-cause mortality Incidence Grp1: 2    Incidence Grp2: 2 |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1480mg) Fixed (45mg daily) Grp2: Metformin + sitagliptin + placebo Fixed (Mean: 1583mg) Fixed (100mg daily) ITT: Yes Followup (wks): 102  NR/unclear | Def:All-cause mortality Incidence Grp1: 1 (0.7)  Incidence Grp2: 2 (1.5) |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1480mg) Fixed (45mg daily) Grp2: Metformin + sitagliptin + placebo Fixed (Mean: 1583mg) Fixed (100mg daily) ITT: Yes Followup (wks): 102  NR/unclear | Def:All-cause mortality Incidence Grp1: 1 (0.7)  Incidence Grp2: 0 (0) |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1480mg) Fixed (45mg daily) Grp2: Metformin + sitagliptin + placebo Fixed (Mean: 1583mg) Fixed (100mg daily) ITT: Yes Followup (wks): 102  NR/unclear | Def:All-cause mortality Incidence Grp1: 1 (0.7)  Incidence Grp2: 0 (0) |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1480mg) Fixed (45mg daily) Grp2: Metformin + sitagliptin + placebo Fixed (Mean: 1583mg) Fixed (100mg daily) ITT: Yes Followup (wks): 104 | Def:All-cause mortality Incidence Grp1: 4 (1)  Incidence Grp2: 4 (1) |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1480mg) Fixed (45mg daily) Grp2: Metformin + exenatide + placebo Fixed (Mean: 1504mg) Fixed (2mg weekly) ITT: No Followup (wks): 24  NR/unclear | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 1 (0.5) |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1480mg) Fixed (45mg daily) Grp2: Metformin + exenatide + placebo Fixed (Mean: 1504mg) Fixed (2mg weekly) ITT: No Followup (wks): 24  NR/unclear | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1480mg) Fixed (45mg daily) Grp2: Metformin + exenatide + placebo Fixed (Mean: 1504mg) Fixed (2mg weekly) ITT: No Followup (wks): 24  NR/unclear | Def:All-cause mortality Incidence Grp1: 1 (0.5)  Incidence Grp2: 0 |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1480mg) Fixed (45mg daily) Grp2: Metformin + exenatide + placebo Fixed (Mean: 1504mg) Fixed (2mg weekly) ITT: Yes Followup (wks): 24 | Def:All-cause mortality Incidence Grp1: 1    Incidence Grp2: 0 |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1480mg) Fixed (45mg daily) Grp2: Metformin + exenatide + placebo Fixed (Mean: 1504mg) Fixed (2mg weekly) ITT: Yes Followup (wks): 24 | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + sitagliptin + placebo Fixed (Mean: 1583mg) Fixed (100mg daily) Grp2: Metformin + exenatide + placebo Fixed (Mean: 1504mg) Fixed (2mg weekly) ITT: Yes Followup (wks): 24 | Def:All-cause mortality Incidence Grp1: 1    Incidence Grp2: 0 |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + sitagliptin + placebo Fixed (Mean: 1583mg) Fixed (100mg daily) Grp2: Metformin + exenatide + placebo Fixed (Mean: 1504mg) Fixed (2mg weekly) ITT: Yes Followup (wks): 24 | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + sitagliptin + placebo Fixed (Mean: 1583mg) Fixed (100mg daily) Grp2: Metformin + exenatide + placebo Fixed (Mean: 1504mg) Fixed (2mg weekly) ITT: Yes Followup (wks): 24 | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + sitagliptin + placebo Fixed (Mean: 1583mg) Fixed (100mg daily) Grp2: Metformin + exenatide + placebo Fixed (Mean: 1504mg) Fixed (2mg weekly) ITT: Yes Followup (wks): 24 | Def:All-cause mortality Incidence Grp1: 1    Incidence Grp2: 0 |  |  |  |
| Bergenstal, 2010[14](#_ENREF_14)  RCT | Grp1: Metformin + sitagliptin + placebo Fixed (Mean: 1583mg) Fixed (100mg daily) Grp2: Metformin + exenatide + placebo Fixed (Mean: 1504mg) Fixed (2mg weekly) ITT: Yes Followup (wks): 24 | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Bolinder, 2012[17](#_ENREF_17)  RCT | Grp1: Metformin + placebo Fixed (Patients continued open-label metformin dosage from prior to enrollment) Grp2: Metformin + dapagliflozin  (Patients continued open-label metformin dosage from prior to enrollment) Fixed (10 mg) ITT: Yes Followup (wks): 24 | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Bolinder, 2012[17](#_ENREF_17)  RCT | Grp1: Metformin + placebo Fixed (Patients continued open-label metformin dosage from prior to enrollment) Grp2: Metformin + dapagliflozin  (Patients continued open-label metformin dosage from prior to enrollment) Fixed (10 mg) ITT: Yes Followup (wks): 102 | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 1 (1.1) |  |  |  |
| Bolinder, 2012[17](#_ENREF_17)  RCT | Grp1: Metformin + placebo Fixed (Patients continued open-label metformin dosage from prior to enrollment) Grp2: Metformin + dapagliflozin  (Patients continued open-label metformin dosage from prior to enrollment) Fixed (10 mg) ITT: Yes Followup (wks): 104  Active | Def:All-cause mortality Incidence Grp1: 4 (1) 408 Persons p  Incidence Grp2: 0 (0) 406 Persons p |  |  |  |
| Borges, 2011[18](#_ENREF_18)  RCT | Grp1: Metformin Titrated (Max: 2000 mg/dStart 500mg/d) Grp2: Metformin + rosiglitazone Titrated (Max: AVM 8mg/2000mgstart AVM 4mg/500mg) Titrated (Max: AVM 8mg/2000mgstart AVM 4mg/500mg) ITT: Yes Followup (wks): 26  Active | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Borges, 2011[18](#_ENREF_18)  RCT | Grp1: Metformin Titrated (Max: 2000 mg/dStart 500mg/d) Grp2: Metformin + rosiglitazone Titrated (Max: AVM 8mg/2000mgstart AVM 4mg/500mg) Titrated (Max: AVM 8mg/2000mgstart AVM 4mg/500mg) ITT: Yes Followup (wks): 26  Active | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 1 |  |  |  |
| Borges, 2011[18](#_ENREF_18)  RCT | Grp1: Metformin Titrated (Max: 2000 mg/dStart 500mg/d) Grp2: Metformin + rosiglitazone Titrated (Max: AVM 8mg/2000mgstart AVM 4mg/500mg) Titrated (Max: AVM 8mg/2000mgstart AVM 4mg/500mg) ITT: Yes Followup (wks): 12 | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Borges, 2011[18](#_ENREF_18)  RCT | Grp1: Metformin Titrated (Max: 2000 mg/dStart 500mg/d) Grp2: Metformin + rosiglitazone Titrated (Max: AVM 8mg/2000mgstart AVM 4mg/500mg) Titrated (Max: AVM 8mg/2000mgstart AVM 4mg/500mg) ITT: Yes Followup (wks): 12 | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Brownstein, 2010[191](#_ENREF_191)  Cohort | Grp1: Metformin  NS  Grp2: Rosiglitazone  NS |  |  | Def: Hospitalization for acute MI  Grp1: ref  Grp2: HR: 3.0 (CI: 2.4-3.7) |  |
| Brownstein, 2010[191](#_ENREF_191)  Cohort | Grp1: Rosiglitazone  NS  Grp2: Sulfonylurea |  |  | Def: Hospitalization for acute MI  Grp1: HR: 1.3 (CI: 1.0-1.7)  Grp2: ref |  |
| Cefalu, 2013[20](#_ENREF_20)  RCT | Grp1: Metformin + glimepiride Fixed (prior metformin dose up-titrated if needed during screening (no change during intervention period after rz reported); seems that goal of >=2000 mg/d ideal but not mandatory) Titrated (Mean: 5.6 mg (mean maximum dose achieved)Max: 6 mg or 8 mg (on the basis of maximum approved dose in the country of the investigational site)) Grp2: Metformin + canagliflozin Fixed (prior metformin dose up-titrated if needed during screening (no change during intervention period after rz reported); seems that goal of >=2000 mg/d ideal but not mandatory) Fixed (100mg) ITT: Yes Followup (wks): 12 | Def:All-cause mortality Incidence Grp1: 0 (0)  Incidence Grp2: 0 (0) |  |  |  |
| Cefalu, 2013[20](#_ENREF_20)  RCT | Grp1: Metformin + glimepiride Fixed (prior metformin dose up-titrated if needed during screening (no change during intervention period after rz reported); seems that goal of >=2000 mg/d ideal but not mandatory) Titrated (Mean: 5.6 mg (mean maximum dose achieved)Max: 6 mg or 8 mg (on the basis of maximum approved dose in the country of the investigational site)) Grp2: Metformin + canagliflozin Fixed (prior metformin dose up-titrated if needed during screening (no change during intervention period after rz reported); seems that goal of >=2000 mg/d ideal but not mandatory) Fixed (300mg) ITT: Yes Followup (wks): 12 | Def:All-cause mortality Incidence Grp1: 0 (0)  Incidence Grp2: 0 (0) |  |  |  |
| Chien, 2007[24](#_ENREF_24)  RCT | Grp1: Metformin  Varied, glucose: 140 mg/dL  Start: 1000mg, Mean: 1910 mg, Max: 2000 mg  D: 4 wks  Grp2: Glyburide  Varied, glucose: 140  Start: 10 mg, Mean: 19 mg, Max: 20 mg  D: 4 wks | Grp1: 0 (0)  Grp2: 0 (0) |  |  |  |
| Chien, 2007[24](#_ENREF_24)  RCT | Grp1: Metformin  Varied, glucose: <140 mg/dL  Start: 1000 mg, Max: 2000 mg, Final mean: 1910 mg  D: 4 wks  Grp2: Metformin + glyburide  Varied, glucose: <140 mg/dL  Start: 1000 mg, Max: 2000 mg, Final mean: 1680 mg; Start: 5 mg, Max: 10 mg, Final mean: 8.4 mg  D: 4 wks | Grp1: 0 (0)  Grp2: 0 (0) |  |  |  |
| Corrao, 2011[192](#_ENREF_192)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 12 | Def:All-cause mortality Incidence Grp1: 0 (0)  Incidence Grp2: 0 (0) |  |  |  |
| Corrao, 2011[192](#_ENREF_192)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 12 | Def:All-cause mortality Incidence Grp1: 0 (0)  Incidence Grp2: 0 (0) |  |  |  |
| DeFronzo, 1995[27](#_ENREF_27)  RCT | Grp1: Metformin  Varied  Start: 500 mg, Max: 2500 mg  Grp2: Glyburide  Varied  Start: 5 mg bid, Max: 10 mg bid | Grp1: 1 (0.5)  Grp2: 0 (0) | Def: CVD mortality/Fatal MI  Grp1: 1 (0.5)  Grp2: 0 (0) |  |  |
| DeFronzo, 1995[27](#_ENREF_27)  RCT | Grp1: Metformin  Varied  Start: 500 mg, Max: 2500 mg  Grp2: Metformin + glyburide  Varied  Start: 500 mg, Max: 2500 mg; Start: 10 mg, Max: 20 mg | Grp1: 1 (1))  Grp2: 0 (0) |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1937mgwas fixed after stabilization/run-in) Grp2: Metformin + pioglitazone + placebo Fixed (Mean: 1893mgfixed dose after run-in) Fixed (15mg) ITT: No Followup (wks): 24 | Def:All-cause mortality Incidence Grp1: 0 (0)  Incidence Grp2: 0 (0) |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1937mgwas fixed after stabilization/run-in) Grp2: Metformin + pioglitazone + placebo Fixed (Mean: 1854mgfixed after run-in) Fixed (30mg) ITT: No Followup (wks): 24 | Def:All-cause mortality Incidence Grp1: 0 (0)  Incidence Grp2: 0 (0) |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1937mgwas fixed after stabilization/run-in) Grp2: Metformin + pioglitazone + placebo Fixed (Mean: 1919mgfixed after run in) Fixed (45mg) ITT: Yes Followup (wks): 12 | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1937mgwas fixed after stabilization/run-in) Grp2: Metformin + pioglitazone + placebo Fixed (Mean: 1893mgfixed dose after run-in) Fixed (15mg) ITT: No Followup (wks): 104  NR/unclear | Def:All-cause mortality Incidence Grp1: 5   Persons p NR  Incidence Grp2: 5   Persons p NR |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1937mgwas fixed after stabilization/run-in) Grp2: Metformin + pioglitazone + placebo Fixed (Mean: 1854mgfixed after run-in) Fixed (30mg) ITT: Yes Followup (wks): 18 | Def:All-cause mortality Incidence Grp1: (0)  Incidence Grp2: (0) |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1937mgwas fixed after stabilization/run-in) Grp2: Metformin + pioglitazone + placebo Fixed (Mean: 1919mgfixed after run in) Fixed (45mg) ITT: Yes Followup (wks): 18 | Def:All-cause mortality Incidence Grp1: (0)  Incidence Grp2: 1 (1.1) |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1937mgwas fixed after stabilization/run-in) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1902mgfixed after run in) Fixed (12.5mg) ITT: No Followup (wks): 24 | Def:All-cause mortality  Incidence Grp1: (0)  Incidence Grp2: (0) |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1937mgwas fixed after stabilization/run-in) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1851mgfixed after run in) Fixed (25mg) ITT: No Followup (wks): 24 | Def:All-cause mortality Incidence Grp1: (0)  Incidence Grp2: (0) |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1937mgwas fixed after stabilization/run-in) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1902mgfixed after run in) Fixed (12.5mg) ITT: No Followup (wks):   NR/unclear | Def:All-cause mortality Incidence Grp1: 0   p  Incidence Grp2: 0   p |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1937mgwas fixed after stabilization/run-in) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1851mgfixed after run in) Fixed (25mg) ITT: No Followup (wks):   NR/unclear | Def:All-cause mortality Incidence Grp1: 0   p  Incidence Grp2: 0   p |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1919mgfixed after run in) Fixed (45mg) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1902mgfixed after run in) Fixed (12.5mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality Incidence Grp1: 23  3246 Person-years p Rate ratio (poisson) 0.77 Incidence Grp2: 304  6916 Person-years p Rate ratio (poisson) 1.95 |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1854mgfixed after run-in) Fixed (30mg) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1902mgfixed after run in) Fixed (12.5mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality Incidence Grp1: 644  31497 Person-years p Rate ratio (poisson) 1 (ref) Incidence Grp2: 23  3246 Person-years p Rate ratio (poisson) 0.77 |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1893mgfixed dose after run-in) Fixed (15mg) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1902mgfixed after run in) Fixed (12.5mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality Incidence Grp1: 644  31497 Person-years p Rate ratio (poisson) 1 (ref) Incidence Grp2: 118  11619 Person-years p Rate ratio (poisson) 0.65 |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1919mgfixed after run in) Fixed (45mg) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1851mgfixed after run in) Fixed (25mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality Incidence Grp1: 644  31497 Person-years p Rate ratio (poisson) 1 (ref) Incidence Grp2: 304  6916 Person-years p Rate ratio (poisson) 1.95 |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1854mgfixed after run-in) Fixed (30mg) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1851mgfixed after run in) Fixed (25mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality Incidence Grp1: 118  11619 Person-years p Rate ratio (poisson) 0.65 Incidence Grp2: 23  3246 Person-years p Rate ratio (poisson) 0.77 |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1893mgfixed dose after run-in) Fixed (15mg) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1851mgfixed after run in) Fixed (25mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality  Incidence Grp1: 118  11619 Person-years p Rate ratio (poisson) 0.65 Incidence Grp2: 304  6916 Person-years p Rate ratio (poisson) 1.95 |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1854mgfixed after run-in) Fixed (30mg) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1902mgfixed after run in) Fixed (12.5mg) ITT: Yes Followup (wks): | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1919mgfixed after run in) Fixed (45mg) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1902mgfixed after run in) Fixed (12.5mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality Incidence Grp1:  222258 Person-years p NR RH 1 Incidence Grp2:  5263 Person-years p NR RH 1.19 (males); 4.36 (1.34-14.20) females) |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1893mgfixed dose after run-in) Fixed (15mg) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1902mgfixed after run in) Fixed (12.5mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality Incidence Grp1:  222258 Person-years p NR RH 1 Incidence Grp2:  47604 Person-years p NR RH 1.55 |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1893mgfixed dose after run-in) Fixed (15mg) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1851mgfixed after run in) Fixed (25mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality Incidence Grp1:  222258 Person-years p NR RH 1 Incidence Grp2:  48238 Person-years p NR RH 1.38 |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1919mgfixed after run in) Fixed (45mg) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1851mgfixed after run in) Fixed (25mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality Incidence Grp1:  47604 Person-years p NR RH 1.55 Incidence Grp2:  5263 Person-years p NR RH 1.19 (males); 4.36 (1.34-14.20) females) |  |  |  |
| DeFronzo, 2012[31](#_ENREF_31)  RCT | Grp1: Metformin + pioglitazone + placebo Fixed (Mean: 1854mgfixed after run-in) Fixed (30mg) Grp2: Metformin + alogliptin + placebo Fixed (Mean: 1851mgfixed after run in) Fixed (25mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality Incidence Grp1:  48238 Person-years p NR RH 1.38 Incidence Grp2:  5263 Person-years p NR RH 1.19 (males); 4.36 (1.34-14.20) females) |  |  |  |
| Del Prato, 2015[32](#_ENREF_32) | Grp1: Metformin + glipizide  Titrated 5,10,20mg  Grp2: Metformin + dapagliflozin  Titrated 2,5,10mg | Def: All-cause mortality  Incidence Grp1: 5 (1.2)  Incidence Grp2: 2 (0.5) |  | Def: Unspecified  Incidence Grp1: 0  Incidence Grp2: 0 |  |
| Del Prato, 2014[33](#_ENREF_33) | Grp1: Metformin + glipizide  Titrated 1823.4 mg  Titrated 5 mg  Grp2: Metformin + alogliptin  Titrated 1825.2 mg  Fixed 12.5 mg | Def: All-cause mortality  Incidence Grp1: 5(0.6)  Incidence Grp2: 3(0.3) | Def: Unspecified  Incidence Grp1: NR(0.5)  Incidence Grp2: NR(0.2) | Def: Composite outcome  Incidence Grp1: NR(1.3)  Incidence Grp2: NR(0.7)  Def: Nonfatal MI  Incidence Grp1: Nr(0.5)  Incidence Grp2: NR(0.1)  Def: Nonfatal stroke  Incidence Grp1: NR(0.3)  Incidence Grp2: NR(0.3) |  |
| Del Prato, 2014[33](#_ENREF_33) | Grp1: Metformin + glipizide  Titrated 1823.4 mg  Titrated 5 mg  Grp2: Metformin + alogliptin  Titrated 1837.2 mg  Fixed 25 mg | Def: All-cause mortality  Incidence Grp1: 5(1.2)  Incidence Grp2: 2(0.5) | Def: Unspecified  Incidence Grp1:NR(0.5)  Incidence Grp2: NR(0.2) | Def: Composite outcome  Incidence Grp1: NR(1.3)  Incidence Grp2: NR(0.9)  Def: Nonfatal MI  Grp1: NR(0.5)  Grp2: NR(0.5)  Def: Nonfatal stroke  Incidence Grp1: NR(0.3)  Incidence Grp2: NR(0.2) |  |
| Diamant, 2010[44](#_ENREF_44)  RCT | Grp1: Metformin + exenatide Not specified (continued stable dose) Fixed (2mg weekly) Grp2: Metformin + insulin glargine Not specified (continued stable dose) Titrated (started at 10 IU per day but adjusted by patient to keep glucose at 4-5.5mmol/L) ITT: Yes Followup (wks): 12  Active | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Diamant, 2010[44](#_ENREF_44)  RCT | Grp1: Metformin + exenatide Not specified (continued stable dose) Fixed (2mg weekly) Grp2: Metformin + insulin glargine Not specified (continued stable dose) Titrated (started at 10 IU per day but adjusted by patient to keep glucose at 4-5.5mmol/L) ITT: Yes Followup (wks): 24  Passive | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Ekstrom, 2012[193](#_ENREF_193)  Retrospective cohort | Grp1: Metformin Not specified (Median: 1100mg) Grp2: Metformin + basal insulin Not specified (Median: 1700mg) Not specified   ITT: Yes Followup (wks): 12 | Def:All-cause mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Ekstrom, 2012[193](#_ENREF_193)  Retrospective cohort | Grp1: Metformin Not specified (Median: 1100mg) Grp2: Metformin + basal insulin Not specified (Median: 1700mg) Not specified   ITT: No Followup (wks): 58 | Def:All-cause mortality Incidence Grp1: 7    Incidence Grp2: 3 |  |  |  |
| Ekstrom, 2012[193](#_ENREF_193)  Retrospective cohort | Grp1: Metformin Not specified (Median: 1100mg)  Grp2: Metformin + basal insulin Not specified (Median: 1700mg) Not specified   ITT: Yes Followup (wks): 144 | Def:All-cause mortality Incidence Grp1: 7   NA p 0.55  Incidence Grp2: 14   NA p |  |  |  |
| Erem, 2014[47](#_ENREF_47)  RCT | Grp1: Metformin Titrated (Max: 2000mg4-8 wks of titration then fixed after that - article reported all patients ended up on 2000 mg) Grp2: Pioglitazone Titrated (Max: 45mg according to glycemic controlinitiated at 15mg/day and titrated in first 4-8 wks then fixed after that (ended up 6 pts on 15 mg, 12 pts on 30 mg and 1 pt on 45 mg)) ITT: Yes Followup (wks): 24  NR/unclear | Def:All-cause mortality Incidence Grp1: 1 (0.7) Persons p  Incidence Grp2: 1 (0.7) Persons p |  |  |  |
| Erem, 2014[47](#_ENREF_47)  RCT | Grp1: Metformin Titrated (Max: 2000mg4-8 wks of titration then fixed after that - article reported all patients ended up on 2000 mg) Grp2: Pioglitazone Titrated (Max: 45mg according to glycemic controlinitiated at 15mg/day and titrated in first 4-8 wks then fixed after that (ended up 6 pts on 15 mg, 12 pts on 30 mg and 1 pt on 45 mg)) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear | Def:All-cause mortality Incidence Grp1: 971   NA p NR RH 1.00 REF Incidence Grp2: 818   NA p NR RH 1.25 |  |  |  |
| Esposito, 2011[48](#_ENREF_48)  RCT | Grp1: Metformin Titrated (Max: 1000mg twice dailyend of titration: 36% on 1500 mg/d and 64% on 2000 mg/d) Grp2: Pioglitazone Titrated (Max: 45 mgend of titration period: 27% on 30 mg/d and 72% on 45 mg/d) ITT: No Followup (wks):   NR/unclear | Def:All-cause mortality Incidence Grp1: 5   Persons p NR  Incidence Grp2: 5   Persons p NR |  |  |  |
| Ferrannini, 2013[194](#_ENREF_194)  RCT | Grp1: Metformin Titrated (Mean: 1567 mg/dayMax: a maximum of 1000 mg twice daily or the maximum tolerated dose1668 mg is mean final dose) Grp2: Empagliflozin Fixed (10mg) ITT: No Followup (wks): 24  NR/unclear | Def:All-cause mortality Incidence Grp1: 0 (0) p  Incidence Grp2: 0 (0) p |  |  |  |
| Ferrannini, 2013[194](#_ENREF_194)  RCT | Grp1: Metformin Titrated (Mean: 1567 mg/dayMax: a maximum of 1000 mg twice daily or the maximum tolerated dose1668 mg is mean final dose) Grp2: Empagliflozin Fixed (25mg) ITT: Not applicable (e.g., cohort) Followup (wks): 114.4 | Def:All-cause mortality Incidence p RH  Incidence p RH 1.64 |  |  |  |
| Ferrannini, 2013[194](#_ENREF_194)  RCT | Grp1: Metformin Titrated (Mean: 1567 mg/dayMax: a maximum of 1000 mg twice daily or the maximum tolerated dose1668 mg is mean final dose) Grp2: Empagliflozin Fixed (10mg) ITT: Not applicable (e.g., cohort) Followup (wks): 114.4 | Def:All-cause mortality Incidence p RH  Incidence p RH 1.59 |  |  |  |
| Ferrannini, 2013[194](#_ENREF_194)  RCT | Grp1: Metformin Titrated (Mean: 1567 mg/dayMax: a maximum of 1000 mg twice daily or the maximum tolerated dose1668 mg is mean final dose) Grp2: Empagliflozin Fixed (25mg) ITT: Not applicable (e.g., cohort) Followup (wks): 114.4 | Def:All-cause mortality Incidence p RH  Incidence p RH 1.68 |  |  |  |
| Ferrannini, 2013[194](#_ENREF_194)  RCT | Grp1: Metformin Titrated (Mean: 1567 mg/dayMax: a maximum of 1000 mg twice daily or the maximum tolerated dose1668 mg is mean final dose) Grp2: Empagliflozin Fixed (10mg) ITT: No Followup (wks): 36  NR/unclear | Def:All-cause mortality Incidence Grp1: 1   p  Incidence p |  |  |  |
| Ferrannini, 2013[194](#_ENREF_194)  RCT | Grp1: Metformin Titrated (Mean: 1567 mg/dayMax: a maximum of 1000 mg twice daily or the maximum tolerated dose1668 mg is mean final dose) Grp2: Empagliflozin Fixed (10mg) ITT: No Followup (wks): 36  NR/unclear | Def:All-cause mortality Incidence Grp1: 1   p  Incidence p |  |  |  |
| Ferrannini, 2013[194](#_ENREF_194)  RCT | Grp1: Metformin Titrated (Mean: 1567 mg/dayMax: a maximum of 1000 mg twice daily or the maximum tolerated dose1668 mg is mean final dose) Grp2: Empagliflozin Fixed (10mg) ITT: No Followup (wks): 36  NR/unclear | Def:All-cause mortality Incidence Grp1: 1   p  Incidence p |  |  |  |
| Ferrannini, 2013[194](#_ENREF_194)  RCT | Grp1: Metformin Titrated (Mean: 1567 mg/dayMax: a maximum of 1000 mg twice daily or the maximum tolerated dose1668 mg is mean final dose) Grp2: Empagliflozin Fixed (25mg) ITT: No Followup (wks): 36  NR/unclear | Def:All-cause mortality  Incidence p  Incidence p |  |  |  |
| Ferrannini, 2013[194](#_ENREF_194)  RCT | Grp1: Metformin Titrated (Mean: 1567 mg/dayMax: a maximum of 1000 mg twice daily or the maximum tolerated dose1668 mg is mean final dose) Grp2: Empagliflozin Fixed (25mg) ITT: No Followup (wks): 36  NR/unclear | Def:All-cause mortality  Incidence p  Incidence p |  |  |  |
| Ferrannini, 2013[194](#_ENREF_194)  RCT | Grp1: Metformin Titrated (Mean: 1567 mg/dayMax: a maximum of 1000 mg twice daily or the maximum tolerated dose1668 mg is mean final dose) Grp2: Empagliflozin Fixed (25mg) ITT: No Followup (wks): 36  NR/unclear | Def:All-cause mortality  Incidence p  Incidence p |  |  |  |
| Fonseca, 2000[55](#_ENREF_55)  RCT | Grp1: Metformin  Fixed  Start: 2500 mg  Grp2: Metformin + rosiglitazone  Fixed  Start: 2500 mg; Start: 8 mg | Grp1: 0 (0)  Grp2: 1 (1) | Def: CVD mortality/unclear mortality + Fatal MI  Grp1: 0 (0)  Grp2: 0 (0) |  |  |
| Fonseca, 2012[56](#_ENREF_56)  RCT | Grp1: Metformin Titrated (Max: 2000 mg/duptitration from 1500 to 2000 mg/d) Grp2: Metformin + saxagliptin Fixed (1500 mg/d) Fixed (5mg/d) ITT: No Followup (wks): 52  NR/unclear | Def:All-cause mortality  Incidence p  Incidence Grp2: 1   p |  |  |  |
| Forst, 2010[57](#_ENREF_57)  RCT | Grp1: Metformin + placebo Fixed (17of 70 patients receiving <1500 mg and 53 of 70 receiving >=1500 mg) Grp2: Metformin + glimepiride Fixed   Titrated (Max: 3 mgstarted from 1mg for 4 wks, thereafter uptitrate the daily dose up to 3mg according to investigator's discretion) ITT: Yes Followup (wks): 24  NR/unclear | Def:All-cause mortality  Incidence p  Incidence p |  |  |  |
| Forst, 2010[57](#_ENREF_57)  RCT | Grp1: Metformin + placebo Fixed (17of 70 patients receiving <1500 mg and 53 of 70 receiving >=1500 mg) Grp2: Metformin + linagliptin Fixed (11 of 62 were on <1500 mg met; 51 of 62 were on >=1500 mg metformin) Fixed (5mg) ITT: No Followup (wks): 80 | Def:All-cause mortality  Incidence Grp1: 1   p  Incidence Grp2: 2   p |  |  |  |
| Forst, 2010[57](#_ENREF_57)  RCT | Grp1: Metformin + glimepiride Fixed   Titrated (Max: 3 mgstarted from 1mg for 4 wks, thereafter uptitrate the daily dose up to 3mg according to investigator's discretion) Grp2: Metformin + linagliptin Fixed (11 of 62 were on <1500 mg met; 51 of 62 were on >=1500 mg metformin) Fixed (5mg) ITT: Not applicable (e.g., cohort) Followup (wks): 91.52  NR/unclear | Def:All-cause mortality  Incidence Grp1: 1548   p RH 1 Incidence Grp2: 1546   p RH 1.19 |  |  |  |
| Gallwitz, 2012[61](#_ENREF_61)  RCT | Grp1: Metformin + glimepiride + placebo Fixed (stable dose of 1500mg per day or more (or a maximum tolerated dose less than 1500mg per day)) Titrated (Mean: 3.0 mgMax: 4 mg once daily) Grp2: Metformin + linagliptin + placebo Fixed (stable dose of 1500mg per day or more (maximum tolerated dose less than 1500mg per day)) Fixed (5 mg once daily) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear | Def:All-cause mortality  Incidence Grp1: 213   p RH 1 Incidence Grp2: 265   p RH 1.47 |  |  |  |
| Gallwitz, 2012[61](#_ENREF_61)  RCT | Grp1: Metformin + glimepiride + placebo Fixed (stable dose of 1500mg per day or more (or a maximum tolerated dose less than 1500mg per day)) Titrated (Mean: 3.0 mgMax: 4 mg once daily) Grp2: Metformin + linagliptin + placebo Fixed (stable dose of 1500mg per day or more (maximum tolerated dose less than 1500mg per day)) Fixed (5 mg once daily) ITT: Not applicable (e.g., cohort) Followup (wks): 91.52  NR/unclear | Def:All-cause mortality  Incidence Grp1: 1548   p RH 1 Incidence Grp2: 947   p RH 1.27 |  |  |  |
| Gallwitz, 2012[61](#_ENREF_61)  RCT | Grp1: Metformin + glimepiride + placebo Fixed (stable dose of 1500mg per day or more (or a maximum tolerated dose less than 1500mg per day)) Titrated (Mean: 3.0 mgMax: 4 mg once daily) Grp2: Metformin + linagliptin + placebo Fixed (stable dose of 1500mg per day or more (maximum tolerated dose less than 1500mg per day)) Fixed (5 mg once daily) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear | Def:All-cause mortality  Incidence Grp1: 213   p RH 1 Incidence Grp2: 141   p RH 1.53 |  |  |  |
| Gallwitz, 2012[61](#_ENREF_61)  RCT | Grp1: Metformin + glimepiride + placebo Fixed (stable dose of 1500mg per day or more (or a maximum tolerated dose less than 1500mg per day)) Titrated (Mean: 3.0 mgMax: 4 mg once daily) Grp2: Metformin + linagliptin + placebo Fixed (stable dose of 1500mg per day or more (maximum tolerated dose less than 1500mg per day)) Fixed (5 mg once daily) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear | Def:All-cause mortality  Incidence Grp1: 213   p RH 1 Incidence Grp2: 737   p RH 1.3 |  |  |  |
| Gallwitz, 2012[61](#_ENREF_61)  RCT | Grp1: Metformin + glimepiride + placebo Fixed (stable dose of 1500mg per day or more (or a maximum tolerated dose less than 1500mg per day)) Titrated (Mean: 3.0 mgMax: 4 mg once daily) Grp2: Metformin + linagliptin + placebo Fixed (stable dose of 1500mg per day or more (maximum tolerated dose less than 1500mg per day)) Fixed (5 mg once daily) ITT: Not applicable (e.g., cohort) Followup (wks): 91.52  NR/unclear | Def:All-cause mortality  Incidence Grp1: 1548   p RH 1 Incidence Grp2: 4081   p RH 1.32 |  |  |  |
| Gallwitz, 2012[61](#_ENREF_61)  RCT | Grp1: Metformin + glimepiride + placebo Fixed (stable dose of 1500mg per day or more (or a maximum tolerated dose less than 1500mg per day)) Titrated (Mean: 3.0 mgMax: 4 mg once daily) Grp2: Metformin + linagliptin + placebo Fixed (stable dose of 1500mg per day or more (maximum tolerated dose less than 1500mg per day)) Fixed (5 mg once daily) ITT: Yes Followup (wks): 44  Active | Def:All-cause mortality  Incidence Grp1: 2 (0.3)  Incidence Grp2: 1 (0.2) |  |  |  |
| Gallwitz, 2012[61](#_ENREF_61)  RCT | Grp1: Metformin + glimepiride + placebo Fixed (stable dose of 1500mg per day or more (or a maximum tolerated dose less than 1500mg per day)) Titrated (Mean: 3.0 mgMax: 4 mg once daily) Grp2: Metformin + linagliptin + placebo Fixed (stable dose of 1500mg per day or more (maximum tolerated dose less than 1500mg per day)) Fixed (5 mg once daily) ITT: Yes Followup (wks): 76 | Def:All-cause mortality  Incidence Grp1: 5 (1.5)  Incidence Grp2: 2 (0.6) |  |  |  |
| Gallwitz, 2012[62](#_ENREF_62)  RCT | Grp1: Metformin + glimepiride Not specified (Mean: 1989 mg) Titrated (Mean: 2.01 mginitial dose 1 mg; could be titrated per attending physician every 4 wks based on maximum tolerated dose and country guidelines) Grp2: Metformin + exenatide Not specified (Mean: 1956 mg) Titrated (Mean: 17.35 micgrogramsMax: 20 microgramsstarted at 5 microgm bid and titrated if possible based on GI sxs) ITT: Yes Followup (wks): 76 | Def:All-cause mortality  Incidence Grp1: 5 (1.5)  Incidence Grp2: 1 (0.3) |  |  |  |
| Garber, 2003[64](#_ENREF_64)  RCT | Grp1: Metformin  Varied  Start: 500 mg, max: 2000 mg  Grp2: Glyburide  Varied  Start: 2.5 mg, max: 10 mg | Grp1: 0 (0)  Grp2: 0 (0) |  |  |  |
| Garber, 2003[64](#_ENREF_64)  RCT | Grp1: Metformin  Varied  Start: 500 mg, Max: 2000 mg  Grp2: Metformin + glyburide  Varied  Start: 500 mg, Max: 2000 mg; Start: 1.25 mg, Max: 20 mg | Grp1: 0 (0)  Grp2: 2 (1) |  |  |  |
| Garber, 2011[67](#_ENREF_67)  RCT | Grp1: Glimepiride + placebo Titrated (Max: 8mg) Grp2: Liraglutide + placebo Titrated (Max: 1.2 mg) ITT: Yes Followup (wks): 76 | Def:All-cause mortality  Incidence Grp1: 5 (1.5)  Incidence Grp2: 2 (0.6) |  |  |  |
| Garber, 2011[67](#_ENREF_67)  RCT | Grp1: Glimepiride + placebo Titrated (Max: 8mg) Grp2: Liraglutide + placebo Titrated (Max: 1.8 mg) ITT: Yes Followup (wks): 76 | Def:All-cause mortality  Incidence Grp1: 2 (0.6)  Incidence Grp2: 1 (0.3) |  |  |  |
| Garber, 2011[67](#_ENREF_67)  RCT | Grp1: Glimepiride + placebo Titrated (Max: 8mg) Grp2: Liraglutide + placebo Titrated (Max: 1.2 mg) ITT: Yes Followup (wks): 76 | Def:All-cause mortality  Incidence Grp1: 2 (0.6)  Incidence Grp2: 2 (0.6) |  |  |  |
| Garber, 2011[67](#_ENREF_67)  RCT | Grp1: Glimepiride + placebo Titrated (Max: 8mg) Grp2: Liraglutide + placebo Titrated (Max: 1.2 mg) ITT: Yes Followup (wks): 24 | Def:All-cause mortality  Incidence Grp1: 0   Persons p NR  Incidence Grp2: 0   Persons p NR |  |  |  |
| Garber, 2011[67](#_ENREF_67)  RCT | Grp1: Glimepiride + placebo Titrated (Max: 8mg) Grp2: Liraglutide + placebo Titrated (Max: 1.8 mg) ITT: Yes Followup (wks): 104  NR/unclear | Def:All-cause mortality  Incidence Grp1: 1    Incidence Grp2: 0 |  |  |  |
| Garber, 2011[67](#_ENREF_67)  RCT | Grp1: Glimepiride + placebo Titrated (Max: 8mg) Grp2: Liraglutide + placebo Titrated (Max: 1.8 mg) ITT: Yes Followup (wks): 104  NR/unclear | Def:All-cause mortality  Incidence Grp1: 1    Incidence Grp2: 1 |  |  |  |
| Garber, 2011[67](#_ENREF_67)  RCT | Grp1: Glimepiride + placebo Titrated (Max: 8mg) Grp2: Liraglutide + placebo Titrated (Max: 1.2 mg) ITT: No Followup (wks): 30 | Def:All-cause mortality  Incidence Grp1: 1   Persons p NR  Incidence Grp2: 0   Persons p NR |  |  |  |
| Garber, 2011[67](#_ENREF_67)  RCT | Grp1: Glimepiride + placebo Titrated (Max: 8mg) Grp2: Liraglutide + placebo Titrated (Max: 1.8 mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality  Incidence p RH  Incidence p RH 1.37 |  |  |  |
| Genovese, 2013[68](#_ENREF_68)  RCT | Grp1: Metformin + placebo Fixed (2550 mg) Grp2: Metformin + pioglitazone Fixed (2550 mg) Fixed (45titrated from 30 mg to 45 mg in first four wks then fixed at 45 for 20 wks) ITT: Yes Followup (wks): 104 | Def:All-cause mortality  Incidence Grp1: 2 (0.5)  Incidence Grp2: 4 (0.9) |  |  |  |
| Genovese, 2013[69](#_ENREF_69)  RCT | Grp1: Metformin Titrated (starting dose of 850mg/day, up-titrated to 1700mg or 2550mg in later visits depending on the glycemic response) Grp2: Pioglitazone + placebo Titrated (Max: 45mgstarting dose of 30mg qd, up-titrated to 45mg qd in later visits in the case of poor response) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear | Def:All-cause mortality  Incidence Grp1: 239 (35) 1533 Person-years p NR 0.85 Incidence Grp2: 2344 (65) 9570 Person-years p NR 1.00 REF |  |  |  |
| Goke, 2010[70](#_ENREF_70)  RCT | Grp1: Metformin + glipizide Fixed (>/= 1500 mgMean: 1883 mg) Titrated (Mean: 14.7 mg/dayMax: 20 mg/day) Grp2: Metformin + saxagliptin  (>/= 1500 mgMean: 1938 mg) Fixed (5 mg Γüä day) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear | Def:All-cause mortality  Incidence Grp1: 239 (35) 1533 Person-years p NR 0.85 Incidence Grp2: 759 (49) 4280 Person-years p NR 0.89 |  |  |  |
| Goke, 2010[70](#_ENREF_70)  RCT | Grp1: Metformin + glipizide Fixed (>/= 1500 mgMean: 1883 mg) Titrated (Mean: 14.7 mg/dayMax: 20 mg/day) Grp2: Metformin + saxagliptin  (>/= 1500 mgMean: 1938 mg) Fixed (5 mg Γüä day) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear | Def:All-cause mortality  Incidence Grp1: 2344 (65) 9570 Person-years p NR 1.00 REF Incidence Grp2: 759 (49) 4280 Person-years p NR 0.89 |  |  |  |
| Goke, 2010[70](#_ENREF_70)  RCT | Grp1: Metformin + glipizide Fixed (>/= 1500 mgMean: 1883 mg) Titrated (Mean: 14.7 mg/dayMax: 20 mg/day) Grp2: Metformin + saxagliptin  (>/= 1500 mgMean: 1938 mg) Fixed (5 mg Γüä day) ITT: Yes Followup (wks): 26 | Def:All-cause mortality  Incidence Grp1: 0 (0)  Incidence Grp2: 0 (0) |  |  |  |
| Goke, 2010[70](#_ENREF_70)  RCT | Grp1: Metformin + glipizide Fixed (>/= 1500 mgMean: 1883 mg) Titrated (Mean: 14.7 mg/dayMax: 20 mg/day) Grp2: Metformin + saxagliptin  (>/= 1500 mgMean: 1938 mg) Fixed (5 mg Γüä day) ITT: No Followup (wks): 26 | Def:All-cause mortality  Incidence Grp1: 0   Persons p  Incidence Grp2: 0   Persons p |  |  |  |
| Goke, 2010[70](#_ENREF_70)  RCT | Grp1: Metformin + glipizide Fixed (>/= 1500 mgMean: 1883 mg) Titrated (Mean: 14.7 mg/dayMax: 20 mg/day) Grp2: Metformin + saxagliptin  (>/= 1500 mgMean: 1938 mg) Fixed (5 mg Γüä day) ITT: Yes Followup (wks): 26  NR/unclear | Def:All-cause mortality  Incidence Grp1:    Incidence Grp2: 1 |  |  |  |
| Goldstein, 2003[71](#_ENREF_71)  RCT | Grp1: Metformin  Varied  Start: 500 mg, Max: 2000 mg  Grp2: Glipizide  Fixed  Start: 15mg bid | Grp1: 0 (0)  Grp2: 0 (0) |  |  |  |
| Goldstein, 2003[71](#_ENREF_71)  RCT | Grp1: Metformin  Varied  Start: 500 mg, Max: 2000 mg  Grp2: Metformin + glipizide  Varied  Start: 500 mg, Max: 2000 mg; Start: 5 mg, Max: 20 mg | Grp1: 0 (0)  Grp2: 0 (0) |  |  |  |
| Gomez-Perez, 2002[73](#_ENREF_73)  RCT | Grp1: Metformin  Fixed  Start: 2500 mg  Grp2: Metformin + rosiglitazone  Fixed  Start: 2500 mg; Start: 2 mg bid |  |  | Def: CVD morbidity/ischemic heart disease + bundle branch block + tachycardia  Grp1: 1 (3)  Grp2: 1 (3) |  |
| Gomez-Perez, 2002[73](#_ENREF_73)  RCT | Grp1: Metformin  Fixed  Start: 2500 mg  Grp2: Metformin + rosiglitazone  Fixed  Start: 2500 mg; Start: 4 mg bid |  |  | Def: CVD morbidity/ischemic heart disease + bundle branch block + tachycardia  Grp1: 1 (3)  Grp2: 2 (5) |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Linagliptin Fixed (5 mg) ITT: Yes Followup (wks): 26  NR/unclear | Def:All-cause mortality  Incidence Grp1:    Incidence Grp2: |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: Linagliptin Fixed (5 mg) ITT: Yes Followup (wks): 26  NR/unclear | Def:All-cause mortality  Incidence Grp1: 1    Incidence Grp2: |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: Linagliptin Fixed (5 mg) ITT: Yes Followup (wks): 104 | Def:All-cause mortality  Incidence Grp1: 0 (0)  Incidence Grp2: 0 (0) |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Linagliptin Fixed (5 mg) ITT: Yes Followup (wks): 104 | Def:All-cause mortality  Incidence Grp1: 1 (0.5)  Incidence Grp2: 0 (0) |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Fixed (1000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 104 | Def:All-cause mortality  Incidence Grp1: 2 (1.1)  Incidence Grp2: 0 (0) |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: Metformin + linagliptin Fixed (1000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 104 | Def:All-cause mortality  Incidence Grp1: 2 (1.1)  Incidence Grp2: 1 (0.6) |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: Metformin + linagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 104 | Def:All-cause mortality  Incidence Grp1: 0 (0)  Incidence Grp2: 1 (0.6) |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 104 | Def:All-cause mortality  Incidence Grp1: 1 (0.5)  Incidence Grp2: 1 (0.6) |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Fixed (1000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 104 | Def:All-cause mortality  Incidence Grp1: 2 (1.1)  Incidence Grp2: 1 (0.6) |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: Metformin + linagliptin Fixed (1000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 104 | Def:All-cause mortality  Incidence Grp1: 1 (0.5)  Incidence Grp2: 1 (0.6) |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: Metformin + linagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 104 | Def:All-cause mortality  Incidence Grp1: 0 (0)  Incidence Grp2: 1 (0.6) |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 104 | Def:All-cause mortality  Incidence Grp1: 0 (0)  Incidence Grp2: 1 (0.6) |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Linagliptin Fixed (5 mg) Grp2: Metformin + linagliptin Fixed (1000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 104 | Def:All-cause mortality  Incidence Grp1: 0 (0)  Incidence Grp2: 1 (0.6) |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Linagliptin Fixed (5 mg) Grp2: Metformin + linagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: Not applicable (e.g., cohort) Followup (wks): | Def:All-cause mortality  Incidence Grp1: 3024 (3.6) p NR RR 1.0 REF Incidence Grp2: 49 (4) p NR RR 1.25 |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Linagliptin Fixed (5 mg)  Grp2: Metformin + linagliptin Fixed (1000 mg) Fixed (5 mg) ITT: No Followup (wks): 24  NR/unclear | Def:All-cause mortality  Incidence Grp1: 1 (0.5)  Incidence Grp2: 0 |  |  |  |
| Haak, 2012[77](#_ENREF_77)  RCT | Grp1: Linagliptin Fixed (5 mg) Grp2: Metformin + linagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: No Followup (wks): 24  NR/unclear | Def:All-cause mortality  Incidence Grp1: 1 (0.5)  Incidence Grp2: 0 |  |  |  |
| Haak, 2013[78](#_ENREF_78)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Fixed (1000 mg) Fixed (5.0 mg) ITT: No Followup (wks): 24  NR/unclear | Def:All-cause mortality  Incidence Grp1: 0    Incidence Grp2: 0 |  |  |  |
| Haak, 2013[78](#_ENREF_78)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 26 |  |  |  | Def:Cerebrovascular Fatal stroke Incidence Grp1: 0  177 Persons p NR  Incidence Grp2: 0  315 Persons p NR |
| Haak, 2013[78](#_ENREF_78)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Fixed (1000 mg) Fixed (5.0 mg) ITT: Yes Followup (wks): 26 |  |  |  | Def:Cerebrovascular Fatal stroke Incidence Grp1: 0  177 Persons p NR  Incidence Grp2: 0  302 Persons p NR |
| Haak, 2013[78](#_ENREF_78)  RCT | Grp1: Metformin Titrated (Max: 2000 mg)    Grp2: Metformin + linagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 26 |  |  |  | Def:Cerebrovascular Fatal stroke Incidence Grp1: 0  177 Persons p NR  Incidence Grp2: 1  304 Persons p NR |
| Haak, 2013[78](#_ENREF_78)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Fixed (1000 mg) Fixed (5.0 mg) ITT: Yes Followup (wks): 26 |  |  |  | Def:Cerebrovascular Fatal stroke Incidence Grp1: 0  315 Persons p NR  Incidence Grp2: 0  302 Persons p NR |
| Haak, 2013[78](#_ENREF_78)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Fixed (1000 mg) Fixed (5.0 mg) ITT: Yes Followup (wks): 26 |  |  |  | Def:Cerebrovascular Fatal stroke Incidence Grp1: 0  315 Persons p NR  Incidence Grp2: 1  304 Persons p NR |
| Haak, 2013[78](#_ENREF_78)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: No Followup (wks): 26  Active |  |  |  | Def:Cerebrovascular Not-fatal stroke (ischemic stroke and cerebrovascular accident) Incidence Grp1: 1 315   Incidence Grp2: |
| Haak, 2013[78](#_ENREF_78)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: No Followup (wks): 26  Active |  |  |  | Def:Cerebrovascular Not-fatal stroke (ischemic stroke and cerebrovascular accident) Incidence Grp1:  1 315  Incidence Grp2: |
| Haak, 2013[78](#_ENREF_78)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Fixed (1000 mg) Fixed (5.0 mg) ITT: No Followup (wks): 26  Active |  |  |  | Def:Cerebrovascular Not-fatal stroke (ischemic stroke and cerebrovascular accident) Incidence Grp1:  1 315  Incidence Grp2:  1 304 |
| Haak, 2013[78](#_ENREF_78)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + linagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: No Followup (wks): 26  Active |  |  |  | Def:Cerebrovascular Not-fatal stroke (ischemic stroke and cerebrovascular accident) Incidence Grp1: 1 315 Incidence Grp2: |
| Hamann, 2008[80](#_ENREF_80)  RCT | Grp1: Metformin + rosiglitazone  Varied, glucose: 6.1 mmol/l  Start: 2 g; Start: 4 mg  D: 12 wks  Grp2: Metformin + sulfonylurea  Varied, glucose: 6.1 mmol/l  Start: 2 g; Start: 5 mg  D: 12 wks | Grp1: 2 (1)  Grp2: 2 (1) |  |  |  |
| Hanefeld, 2004[81](#_ENREF_81)  RCT | Grp1: Metformin + sulfonylurea  Varied; NR  Start: 850 mg, Max: 850 mg tid; NR  Grp2: Pioglitazone + sulfonylurea  Varied; NR  Start: 15 mg, Max: 45 mg; NR | Grp1: 2 (1)  Grp2: 1 (<1) |  | Def: Coronary heart diseases/cardiac disorders  Grp1: (3.1)  Grp2: (4.1) |  |
| Hanefeld, 2007[82](#_ENREF_82)  RCT | Grp1: Rosiglitazone  Fixed  Start: 4 mg  D: 12 wks  Grp2: Glibenclamide  Varied  Start: 2.5 mg, Max: 15 mg  D: 12 wks | Grp1: 0 (0)  Grp2: 0 (0) |  |  |  |
| Hanefeld, 2007[82](#_ENREF_82)  RCT | Grp1: Rosiglitazone  Fixed  Start: 8 mg  D: 12 wks  Grp2: Glibenclamide  Varied  Start: 2.5 mg, Max: 15 mg  D: 12 wks | Grp1: 0 (0)  Grp2: 0 (0) |  |  |  |
| Haring, 2014[83](#_ENREF_83)  RCT | Grp1: Metformin + placebo Not specified (prior MFM therapy (>=1500mg/day, max tolerated dose or max dose according to local label)) Grp2: Metformin + empagliflozin Not specified (prior MFM therapy (>=1500mg/day, max tolerated dose or max dose according to local label)) Fixed (10mg) ITT: No Followup (wks): 26  Active |  |  |  | Def:Cerebrovascular Not-fatal stroke (ischemic stroke and cerebrovascular accident) Incidence Grp1:    Incidence Grp2: |
| Haring, 2014[83](#_ENREF_83)  RCT | Grp1: Metformin + placebo Not specified (prior MFM therapy (>=1500mg/day, max tolerated dose or max dose according to local label)) Grp2: Metformin + empagliflozin Not specified (prior MFM therapy (>=1500mg/day, max tolerated dose or max dose according to local label)) Fixed (25mg) ITT: No Followup (wks): 26  Active |  |  |  | Def:Cerebrovascular Not-fatal stroke (ischemic stroke and cerebrovascular accident) Incidence Grp1:    Incidence Grp2: |
| Henry, 2012[84](#_ENREF_84)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1843.6 mgMedian: 2000 mgMax: 2000mg) Grp2: Dapagliflozin + placebo Fixed (5mg) ITT: No Followup (wks): 26  Active |  |  |  | Def:Cerebrovascular Not-fatal stroke (ischemic stroke and cerebrovascular accident) Incidence Grp1:    Incidence Grp2: |
| Henry, 2012[84](#_ENREF_84)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1843.6 mgMedian: 2000 mgMax: 2000mg) Grp2: Metformin + dapagliflozin Titrated (Mean: 1773.5 mgMax: 2000mg) Fixed (5 mg) ITT: No Followup (wks): 26  Active |  |  |  | Def:Cerebrovascular Not-fatal stroke (ischemic stroke and cerebrovascular accident) Incidence Grp1:    Incidence Grp2: |
| Henry, 2012[84](#_ENREF_84)  RCT | Grp1: Dapagliflozin + placebo Fixed (5mg) Grp2: Metformin + dapagliflozin Titrated (Mean: 1773.5 mgMax: 2000mg) Fixed (5 mg) ITT: Yes Followup (wks): 52  Passive |  |  |  | Def:Cerebrovascular Not-fatal stroke (non-fatal stroke) Incidence Grp1: 1    Incidence Grp2: 1 |
| Henry, 2012[84](#_ENREF_84)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1949.7 mgMedian: 2000 mgMax: 2000 mg)   Grp2: Dapagliflozin + placebo Fixed (10 mg)  ITT: Yes Followup (wks): 52  Passive |  |  |  | Def:Cerebrovascular Not-fatal stroke (non-fatal stroke) Incidence Grp1: 1    Incidence Grp2: |
| Henry, 2012[84](#_ENREF_84)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1949.7 mgMedian: 2000 mgMax: 2000 mg) Grp2: Metformin + dapagliflozin Titrated (Mean: 1928.6 mgMedian: 2000 mgMax: 2000 mg) Fixed (10 mg) ITT: Yes Followup (wks): 104 |  |  |  | Def:Cerebrovascular Other cerebrovascular (cerebral infarction) Incidence Grp1: 4 (0.5)  Incidence Grp2: 0 (0) |
| Henry, 2012[84](#_ENREF_84)  RCT | Grp1: Dapagliflozin + placebo Fixed (10 mg) Grp2: Metformin + dapagliflozin Titrated (Mean: 1928.6 mgMedian: 2000 mgMax: 2000 mg) Fixed (10 mg) ITT: Yes Followup (wks): 104 |  |  |  | Def:Cerebrovascular Not-fatal stroke (not defined) Incidence Grp1: 11   NA p NR RR  Incidence Grp2: 3   NA p NR RR 0.27 |
| Hermann, 1994[86](#_ENREF_86)  RCT | Grp1: Metformin  Varied  Start: 1000 mg, Max: 3000 mg  Grp2: Glyburide  Varied  Start: 3.5 mg, Max: 10.5 mg |  |  | Def: CVD morbidity/unclear CHD  Grp1: 2 (5)  Grp2: 3 (9) |  |
| Hermann, 1994[86](#_ENREF_86)  RCT | Grp1: Metformin  Varied  Start: 1000 mg, Max: 3000 mg  Grp2: Metformin + glyburide  Varied  Start: 500 mg, Max: 1500 mg; Start: 1.75mg, Max: 5.25 mg |  |  | Def: CVD morbidity/unclear CHD  Grp1: 2( 5)  Grp2: 10 (14) |  |
| Hermans, 2012[87](#_ENREF_87)  RCT | Grp1: Metformin Titrated (1500mgMean: mean additional dose (on top of 1500 mg) was 904 mgadded 500mg qd or bid depending on clinical determination) Grp2: Metformin + saxagliptin Fixed (1500 mg) Fixed (5 mg) ITT: No Followup (wks): 26  NR/unclear |  |  |  | Def:Cerebrovascular Not-fatal stroke (cerebrovascular accident, not defined) Incidence Grp1: 1    Incidence Grp2: |
| Home, 2009[89](#_ENREF_89)  RCT | Grp1: Metformin + sulfonylurea  Varied, HgbA1c: ≤7.0%  Max: 2550 mg;  Glibenclamide, Max: 15 mg, Glimepiride, Max: 4 mg  D: 8 wks  Grp2: Rosiglitazone + metformin or sulfonylurea  Varied, HgbA1c: ≤7.0%  Start: 4 mg, Max: 8 mg; Metformin, Max: 2550 mg, Glibenclamide, Max: 15 mg, Glimepiride, Max: 4 mg  D: 8 wks | Grp1: 157  Grp2: 136  HR: 0.86 (CI: 0.68 to 1.08), p: 0.19 | Grp1: 71  Grp2: 60  HR: 0.84 (CI: 0.59 to 1·18), p: 0.32 | Def: Fatal and non-fatal MI  Grp1: 56  Grp2: 64  HR: 1.14 (CI: 0.80 to 1·63), p: 0.47 | Def: Fatal and non-fatal stroke  Grp1: 63  Grp2: 46  HR: 0.72 (CI: 0.49 to 1·06), p: 0.10 |
| Hong, 2013[195](#_ENREF_195)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1.4gMax: 1.5ginitial dose was 0.75g, titrated to 1.5g within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) Grp2: Glipizide + placebo Titrated (Mean: 28.3mgMax: 30mginitial dose was 15mg, titrated to 30 mg within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l))    ITT: No Followup (wks): 26  NR/unclear |  |  |  | Def:Cerebrovascular Not-fatal stroke (cerebrovascular accident, not defined) Incidence Grp1: 1    Incidence Grp2: |
| Hong, 2013[195](#_ENREF_195)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1.4gMax: 1.5ginitial dose was 0.75g, titrated to 1.5g within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) Grp2: Glipizide + placebo Titrated (Mean: 28.3mgMax: 30mginitial dose was 15mg, titrated to 30 mg within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) ITT: No Followup (wks): 26  NR/unclear |  |  |  | Def:Cerebrovascular Not-fatal stroke (cerebrovascular accident, not defined) Incidence Grp1: 1    Incidence Grp2: |
| Hong, 2013[195](#_ENREF_195)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1.4gMax: 1.5ginitial dose was 0.75g, titrated to 1.5g within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) Grp2: Glipizide + placebo Titrated (Mean: 28.3mgMax: 30mginitial dose was 15mg, titrated to 30 mg within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) ITT: No Followup (wks): 26  NR/unclear |  |  |  | Def:Cerebrovascular Not-fatal stroke (cerebrovascular accident, not defined) Incidence Grp1: 1    Incidence Grp2: |
| Hong, 2013[195](#_ENREF_195)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1.4gMax: 1.5ginitial dose was 0.75g, titrated to 1.5g within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) Grp2: Glipizide + placebo Titrated (Mean: 28.3mgMax: 30mginitial dose was 15mg, titrated to 30 mg within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) ITT: No Followup (wks): 26  NR/unclear |  |  |  | Def:Cerebrovascular Not-fatal stroke (cerebrovascular accident, not defined) Incidence Grp1: 1    Incidence Grp2: |
| Hong, 2013[195](#_ENREF_195)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1.4gMax: 1.5ginitial dose was 0.75g, titrated to 1.5g within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) Grp2: Glipizide + placebo Titrated (Mean: 28.3mgMax: 30mginitial dose was 15mg, titrated to 30 mg within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) ITT: No Followup (wks): 26  NR/unclear |  |  |  | Def:Cerebrovascular Not-fatal stroke (cerebrovascular accident, not defined) Incidence Grp1:    Incidence Grp2: |
| Hong, 2013[195](#_ENREF_195)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1.4gMax: 1.5ginitial dose was 0.75g, titrated to 1.5g within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) Grp2: Glipizide + placebo Titrated (Mean: 28.3mgMax: 30mginitial dose was 15mg, titrated to 30 mg within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) ITT: No Followup (wks): 26  NR/unclear |  |  |  | Def:Cerebrovascular Not-fatal stroke (cerebrovascular accident, not defined) Incidence Grp1:    Incidence Grp2: |
| Hong, 2013[195](#_ENREF_195)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1.4gMax: 1.5ginitial dose was 0.75g, titrated to 1.5g within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l))    Grp2: Glipizide + placebo Titrated (Mean: 28.3mgMax: 30mginitial dose was 15mg, titrated to 30 mg within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l))    ITT: No Followup (wks): 26  NR/unclear |  |  |  | Def:Cerebrovascular Not-fatal stroke (cerebrovascular accident, not defined) Incidence Grp1:    Incidence Grp2: |
| Hong, 2013[195](#_ENREF_195)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1.4gMax: 1.5ginitial dose was 0.75g, titrated to 1.5g within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) Grp2: Glipizide + placebo Titrated (Mean: 28.3mgMax: 30mginitial dose was 15mg, titrated to 30 mg within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) ITT: No Followup (wks): 26  NR/unclear |  |  |  | Def:Cerebrovascular Not-fatal stroke (cerebrovascular accident, not defined) Incidence Grp1:    Incidence Grp2: |
| Hong, 2013[195](#_ENREF_195)  RCT | Grp1: Metformin + placebo Titrated (Mean: 1.4gMax: 1.5ginitial dose was 0.75g, titrated to 1.5g within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) Grp2: Glipizide + placebo Titrated (Mean: 28.3mgMax: 30mginitial dose was 15mg, titrated to 30 mg within 3 months if not to target (HbA1c<7.0%, FBG concentration < 7mmol/l, postload 2-h BG < 10mmol/l)) ITT: No Followup (wks): 26  NR/unclear |  |  |  | Def:Cerebrovascular Not-fatal stroke (cerebrovascular accident, not defined) Incidence Grp1:    Incidence Grp2: |
| Horsdal, 2011[196](#_ENREF_196)  Case-control | Grp1: Metformin Not specified   Grp2: SU Not specified    ITT: No Followup (wks): 26  NR/unclear |  |  |  | Def:Cerebrovascular Not-fatal stroke (cerebrovascular accident, not defined) Incidence Grp1:    Incidence Grp2: |
| Hsiao, 2009[215](#_ENREF_215)  Cohort | Grp1: Metformin  NS  Grp2: Pioglitazone  NS |  |  | Def: Angina pectoris defined by ICD-9-CM diagnostic codes for hospitalization  Grp1: 1367 (2.97)  Grp2: 22 (4.51) HR: 1.15 (CI: 0.6 to 2.21) p: 0.6753  Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 484 (1.02)  Grp2: 44 (8.89) HR: 1.0 (CI: 0.26 to 3.89) p: 0.9954 | Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 116 (0.25)  Grp2: 2 (0.41)  Def: TIA defined by ICD-9-CM diagnostic codes of hospitalization  Grp1: 285 (0.63)  Grp2: 5 (1.03) |
| Hsiao, 2009[215](#_ENREF_215)  Cohort | Grp1: Metformin  NS  Grp2: Rosiglitazone  NS |  |  | Def: Angina pectoris defined by ICD-9-CM diagnostic codes for hospitalization  Grp1: 1367 (2.97)  Grp2: 154 (7.52) HR: 1.79 (CI: 1.39 to 2.3)  Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 484 (1.02)  Grp2: 266 (12.71) HR: 2.09 (CI: 1.36 to 3.24) p: 0.0007 | Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 116 (0.25)  Grp2: 16 (0.8)  Def: TIA defined by ICD-9-CM diagnostic codes of hospitalization  Grp1: 285 (0.63)  Grp2: 23 (1.14) |
| Hsiao, 2009[215](#_ENREF_215)  Cohort | Grp1: Metformin  NS  Grp2: Sulfonylurea  NS |  |  | Def: Angina pectoris defined by ICD-9-CM diagnostic codes for hospitalization  Grp1: 1367 (2.97)  Grp2: 3721 (3.87)  Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 484 (1.02)  Grp2: 1678 (1.76) | Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 116 (0.25)  Grp2: 318 (0.34)  Def: TIA defined by ICD-9-CM diagnostic codes of hospitalization  Grp1: 285 (0.63)  Grp2: 940 (0.99) |
| Hsiao, 2009[215](#_ENREF_215)  Cohort | Grp1: Metformin  NS  Grp2: Metformin + rosiglitazone  NS |  |  | Def: Angina pectoris defined by ICD-9-CM diagnostic codes for hospitalization  Grp1: 1367 (2.97)  Grp2: 103 (4.26)  Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 484 (1.02)  Grp2: 25 (1.03) | Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 116 (0.25)  Grp2: 12 (0.49)  Def: TIA defined by ICD-9-CM diagnostic codes of hospitalization  Grp1: 285 (0.63)  Grp2: 11 (0.45) |
| Hsiao, 2009[215](#_ENREF_215)  Cohort | Grp1: Metformin  NS  Grp2: Metformin + sulfonylurea  NS |  |  | Def: Angina pectoris defined by ICD-9-CM diagnostic codes for hospitalization  Grp1: 1367 (2.97)  Grp2: 5910 (2.2)  Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 484 (1.02)  Grp2: 11435 (4.27) | Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 116 (0.25)  Grp2: 588 (0.22)  Def: TIA defined by ICD-9-CM diagnostic codes of hospitalization  Grp1: 285 (0.63)  Grp2: 1637 (0.61) |
| Hsiao, 2009[215](#_ENREF_215)  Cohort | Grp1: Rosiglitazone  NS  Grp2: Pioglitazone  NS |  |  | Def: Angina pectoris defined by ICD-9-CM diagnostic codes for hospitalization  Grp1: 154 (7.52)  Grp2: 22 (4.51)  Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 266 (12.71)  Grp2: 44 (8.89) | Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 16 (0.8)  Grp2: 2 (0.41)  Def: TIA defined by ICD-9-CM diagnostic codes of hospitalization  Grp1: 23 (1.14)  Grp2: 5 (1.03) |
| Hsiao, 2009[215](#_ENREF_215)  Cohort | Grp1: Pioglitazone  NS  Grp2: Sulfonylurea  NS |  |  | Def: Angina pectoris defined by ICD-9-CM diagnostic codes for hospitalization  Grp1: 22 (4.51)  Grp2: 3721 (3.87)  Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 44 (8.89)  Grp2: 1678 (1.76) | Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 2 (0.41)  Grp2: 318 (0.34)  Def: TIA defined by ICD-9-CM diagnostic codes of hospitalization  Grp1: 5 (1.03)  Grp2: 940 (0.99) |
| Hsiao, 2009[215](#_ENREF_215)  Cohort | Grp1: Rosiglitazone  NS  Grp2: Sulfonylurea  NS |  |  | Def: Angina pectoris defined by ICD-9-CM diagnostic codes for hospitalization  Grp1: 154 (7.52)  Grp2: 3721 (3.87)  Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 266 (12.71)  Grp2: 1678 (1.76) | Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 16 (0.8)  Grp2: 318 (0.34)  Def: TIA defined by ICD-9-CM diagnostic codes of hospitalization  Grp1: 23 (1.14)  Grp2: 940 (0.99) |
| Hsiao, 2009[215](#_ENREF_215)  Cohort | Grp1: Metformin + rosiglitazone  NS  Grp2: Metformin + sulfonylurea  NS |  |  | Def: Angina pectoris defined by ICD-9-CM diagnostic codes for hospitalization  Grp1: 103 (4.26)  Grp2: 5910 (2.2)  Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 25 (1.03)  Grp2: 11435 (4.27) | Def: ICD-9-CM diagnostic codes of hospitalization  Grp1: 12 (0.49)  Grp2: 588 (0.22)  Def: TIA defined by ICD-9-CM diagnostic codes of hospitalization  Grp1: 11 (0.45)  Grp2: 1637 (0.61) |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Rosiglitazone Not specified   ITT: Yes Followup (wks): 24 |  |  |  | Def:Cerebrovascular Other cerebrovascular (transient ischemic attack NOS) Incidence Grp1:    Incidence Grp2: 1   NA p NR |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Rosiglitazone Not specified   ITT: NR Followup (wks): 24  NR/unclear |  |  |  | Def:Cerebrovascular Other cerebrovascular (CVA) Incidence Grp1:    Incidence Grp2: 1 |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Rosiglitazone Not specified      ITT: NR Followup (wks): 24  NR/unclear |  |  |  | Def:Cerebrovascular Other cerebrovascular (CVA) Incidence Grp1:    Incidence Grp2: |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Rosiglitazone Not specified   ITT: Yes Followup (wks): 144 |  |  |  | Def:Cerebrovascular Not-fatal stroke (no specific definition but confirmed by medical record) Incidence Grp1: 10    Incidence Grp2: 15 |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Rosiglitazone Not specified    ITT: Yes Followup (wks): 168 |  |  |  | Def:Cerebrovascular Other cerebrovascular (cerebrovascular incident) Incidence Grp1:    Incidence Grp2: 1 (4) |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: No Followup (wks): 80 |  |  |  | Def:Cerebrovascular Other cerebrovascular (not clearly predefined (just said 'cerebrovascular events'stem infarction) Incidence Grp1: 3   Persons p  Incidence Grp2: 5 (1) Persons p |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 76 |  |  |  | Def:Cerebrovascular Other cerebrovascular (death due to ischemic stroke or cerebrovascular accident) Incidence Grp1: 1   p  Incidence Grp2: 1   p |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 76 |  |  |  | Def:Cerebrovascular Other cerebrovascular (death due to ischemic stroke or cerebrovascular accident) Incidence Grp1: 1   p  Incidence p |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 76 |  |  |  | Def:Cerebrovascular Other cerebrovascular (death due to ischemic stroke or cerebrovascular accident) Incidence Grp1: 1   p  Incidence p |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 76 |  |  |  | Def:Cerebrovascular Other cerebrovascular (death due to ischemic stroke or cerebrovascular accident) Incidence Grp1: 1   p  Incidence p |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: SU Not specified   Grp2: Rosiglitazone Not specified   ITT: Yes Followup (wks): 76 |  |  |  | Def:Cerebrovascular Other cerebrovascular (death due to ischemic stroke or cerebrovascular accident) Incidence Grp1: 1   p  Incidence p |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: SU Not specified   Grp2: Rosiglitazone Not specified   ITT: No Followup (wks): 30 |  |  |  | Def:Cerebrovascular Fatal stroke Incidence Grp1: 1   p  Incidence p |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: SU Not specified   Grp2: Rosiglitazone Not specified   ITT: Yes Followup (wks): 104 |  |  |  | Def:Cerebrovascular Other cerebrovascular (transient ischemic attack) Incidence Grp1: 1    Incidence Grp2: |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: SU Not specified   Grp2: Rosiglitazone Not specified   ITT: Yes Followup (wks): 104 |  |  |  | Def:Cerebrovascular Fatal stroke Incidence Grp1: 1    Incidence Grp2: |
| Hung, 2012[198](#_ENREF_198)  Retrospective cohort | Grp1: SU Not specified   Grp2: Rosiglitazone Not specified   ITT: No Followup (wks): 26 |  |  |  | Def:Cerebrovascular Other cerebrovascular (Cerebrovascular accident) Incidence Grp1: 1 (1) Persons p  Incidence Grp2: 1 (1) Persons p |
| Hung, 2013[199](#_ENREF_199)  Retrospective cohort | Grp1: Metformin Not specified    Grp2: Glyburide Not specified   ITT: No Followup (wks): 26 |  |  |  | Def:Cerebrovascular Other cerebrovascular (Cerebrovascular accident) Incidence Grp1: 1 (1) Persons p  Incidence Grp2: 0 (0) Persons p |
| Hung, 2013[199](#_ENREF_199)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Glimepiride Not specified   ITT: No Followup (wks): 26 |  |  |  | Def:Cerebrovascular Other cerebrovascular (Cerebrovascular accident) Incidence Grp1: 1 (1) Persons p  Incidence Grp2: 0 (0) Persons p |
| Hung, 2013[200](#_ENREF_200)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: No Followup (wks): 26  Active |  |  | Def:CVD morbidity Nonfatal MI (unspecified) Incidence Grp1:    Incidence Grp2: 1 |  |
| Hung, 2013[200](#_ENREF_200)  Retrospective cohort | Grp1: Metformin Not specified    Grp2: SU Not specified   ITT: No Followup (wks): 26  Active |  |  | Def:CVD morbidity Nonfatal MI (unspecified) Incidence Grp1:    Incidence Grp2: 1 |  |
| Hung, 2013[200](#_ENREF_200)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: No Followup (wks): 26  Active |  |  | Def:CVD morbidity Nonfatal MI (unspecified) Incidence Grp1:    Incidence Grp2: |  |
| Hung, 2013[200](#_ENREF_200)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Metformin + su Not specified   Not specified   ITT: No Followup (wks): 26  Active |  |  | Def:CVD morbidity Nonfatal MI (unspecified) Incidence Grp1:    Incidence Grp2: |  |
| Hung, 2013[200](#_ENREF_200)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Metformin + su Not specified   Not specified   ITT: No Followup (wks): 26  Active |  |  | Def:CVD morbidity Nonfatal MI (unspecified) Incidence Grp1:    Incidence Grp2: |  |
| Hung, 2013[200](#_ENREF_200)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Metformin + su Not specified   Not specified   ITT: No Followup (wks): 26  Active |  |  | Def:CVD morbidity Nonfatal MI (unspecified) Incidence Grp1:    Incidence Grp2: |  |
| Hung, 2013[200](#_ENREF_200)  Retrospective cohort | Grp1: SU Not specified   Grp2: Metformin + su Not specified   Not specified   ITT: No Followup (wks): 26  Active |  |  | Def:CVD morbidity Nonfatal MI (unspecified) Incidence Grp1:    Incidence Grp2: 1 |  |
| Hung, 2013[200](#_ENREF_200)  Retrospective cohort | Grp1: SU Not specified   Grp2: Metformin + su Not specified   Not specified   ITT: No Followup (wks): 26  Active |  |  | Def:CVD morbidity Nonfatal MI (unspecified) Incidence Grp1:    Incidence Grp2: 1 |  |
| Hung, 2013[200](#_ENREF_200)  Retrospective cohort | Grp1: SU Not specified   Grp2: Metformin + su Not specified   Not specified   ITT: Yes Followup (wks): 52  Active |  |  | Def:CVD morbidity Nonfatal MI (non-fatal MI) Incidence Grp1: 1    Incidence Grp2: 3 |  |
| Jadzinsky, 2009[91](#_ENREF_91)  RCT | Grp1: Metformin  Varied, NS  Start: 500 mg, Max: 1000 mg  D: 1 week  Gpr2: Saxagliptin  Fixed | Grp1: 3 (1)  Grp2: 0 (0) |  |  |  |
| Jadzinsky, 2009[91](#_ENREF_91)  RCT | Grp1: Metformin + saxagliptin  Varied, prespecified target dose; Fixed  Start: 500 mg, Max: 1000 mg; Mean: 10 mg  D: 1 week  Grp2: Metformin  Varied, NS  Start: 500 mg, Max: 1000 mg  D: 1 week | Grp1: 0 (0)  Grp2: 3 (1) |  |  |  |
| Jadzinsky, 2009[91](#_ENREF_91)  RCT | Grp1: Metformin + saxagliptin  Varied, prespecified target dose; Fixed  Start: 500 mg, Max: 1000 mg; Mean: 5 mg  Grp2: Metformin  Varied, NS  Start: 500 mg, Max: 1000 mg  D: 1 week | Grp1: 0 (0)  Grp2: 3 (1) |  |  |  |
| Jain, 2006[92](#_ENREF_92)  RCT | Grp1: Pioglitazone  Varied, glucose: 69-141 mg/dL  Start: 15 mg, Median: 45 mg, Max: 45 mg  D: 12 wks  Grp2: Glyburide  Varied, glucose: 69-141 mg/dL  Start: 5 mg, Median: 10 mg, Max: 15 mg  D: 12 wks | Grp1: 0 (0)  Grp2: 2 (0.8) |  | Def: Non-fatal MI  Grp1: 2 (0.8)  Grp2: 2 (0.8) |  |
| Johnson, 2005[201](#_ENREF_201)  Cohort | Grp1: Metformin  Varied  Min: 250 mg  Grp2: Sulfonylurea  Varied |  | Def: CVD mortality/CVD mortality registry + CVD mortality + ICD-9 codes 410, 411-414, 420-427, 429, 428, 430-432, 433-434, 436-438, 440  Grp1: 14.4/1000 patient-years  Grp2: 25.5/1000 patient-years | Def: Non-fatal cardiovascular hospitalization/used ICD-9 codes 410-414, 420-427, 429, 428, 440, 430-432, 433-434, 436-438  Grp1: 53.7/1000 patient-years  Grp2: 75.3/1000 patient-years |  |
| Jones, 2003[202](#_ENREF_202)  RCT | Grp1: Metformin  Fixed  Start: 2.5 g  Grp2: Metformin + rosiglitazone  Fixed; Varied, NS  Start: 2.5 g; Max: 8 mg | Grp1: 0 (0)  Grp2: 1 (1) |  |  |  |
| Kadowaki, 2013[96](#_ENREF_96)  RCT | Grp1: Metformin + placebo Fixed (maintained previous dosage40% on 500 mg/day; 56% on 750 mg/day; 3% on 1000 mg/day; 1.4% on 1500 mg/day) Grp2: Metformin + sitagliptin Fixed (maintained previous dosage43% on 500 mg/day; 51% on 750 mg/day; 3% on 1000mg/day; 4% on 1500 mg/day) Fixed (50mg qd) ITT: Yes Followup (wks): 52  Active |  |  | Def:CVD morbidity Other CVD morbidity (unstable angina) Incidence Grp1:    Incidence Grp2: 2 |  |
| Kadowaki, 2013[96](#_ENREF_96)  RCT | Grp1: Metformin + placebo Fixed (maintained previous dosage40% on 500 mg/day; 56% on 750 mg/day; 3% on 1000 mg/day; 1.4% on 1500 mg/day) Grp2: Metformin + sitagliptin Fixed (maintained previous dosage43% on 500 mg/day; 51% on 750 mg/day; 3% on 1000mg/day; 4% on 1500 mg/day) Fixed (50mg qd) ITT: Yes Followup (wks): 52  Active |  |  | Def:CVD morbidity Nonfatal MI (non-fatal MI) Incidence Grp1: 1    Incidence Grp2: |  |
| Kahler, 2007[203](#_ENREF_203)  Cohort | Grp1: Metformin  NR  Grp2: Sulfonylurea  NR | Grp1: 82 (2.7)  Grp2: 1005 (5.3) |  |  |  |
| Kahler, 2007[203](#_ENREF_203)  Cohort | Grp1: Metformin  NR  Grp2: Metformin + sulfonylurea  NR | Grp1: 82 (2.7)  Grp2: 468 (3.4) |  |  |  |
| Kahn, 2006[97](#_ENREF_97)  RCT | Grp1: Metformin  Varied, glucose: 140 mg/dL  Start: 500 mg, Max: 2000 mg  Grp2: Rosiglitazone  Varied, glucose: 140 mg/dL  Start: 4 mg, Max: 8 mg | Grp1: 31 (2)  Grp2: 34 (2) | Def: Fatal MI  Grp1: 2 (0.1)  Grp2: 2 (0.1) | Grp1: 21 (1.4)  Grp2: 25 (1.7) | Def: Stroke not defined  Grp1: 19 (1.3)  Grp2: 16 (1.1) |
| Kahn, 2006[97](#_ENREF_97)  RCT | Grp1: Metformin  Varied, glucose: 140 mg/dL  Start: 500 mg, Max: 2000 mg  Grp2: Glyburide  Varied, glucose: 140 mg/dL  Start: 2.5 mg, Max: 15 mg | Grp1: 31 (2)  Grp2: 31 (2) | Def: Fatal MI  Grp1: 2 (0.1)  Grp2: 3 (0.2) | Def: Not defined  Grp1: 21 (1.4)  Grp2: 15 (1) | Def: Stroke not defined  Grp1: 19 (1.3)  Grp2: 17 (1.2) |
| Kahn, 2006[97](#_ENREF_97)  RCT | Grp1: Rosiglitazone  Varied, glucose: 140 mg/dL  Start: 4 mg, Max: 8 mg  Grp2: Glyburide  Varied, glucose: 140 mg/dL  Start: 2.5 mg, Max: 15 mg | Grp1: 34 (2)  Grp2: 31 (2) | Def: Fatal MI  Grp1: 2 (0.1)  Grp2: 3 (0.2) | Def: Non-fatal MI  Grp1: 25 (1.7)  Grp2: 15 (1) | Def: Stroke not defined  Grp1: 16 (1.1)  Grp2: 17 (1.2) |
| Kaku, 2011[99](#_ENREF_99)  RCT | Grp1: Glibenclamide Fixed (1.25 -2.5 mg/d) Grp2: Liraglutide Titrated (Max: 0.9 mg/d) ITT: Yes Followup (wks): 52  Active |  |  | Def:CVD morbidity Other CVD morbidity (unstable angina) Incidence Grp1:    Incidence Grp2: 2 |  |
| Kaku, 2011[99](#_ENREF_99)  RCT | Grp1: Glibenclamide Fixed (1.25 -2.5 mg/d) Grp2: Liraglutide Titrated (Max: 0.9 mg/d) ITT: No Followup (wks): 26 |  |  | Def:CVD morbidity CVD morbidity composite outcome (see comments) Incidence p  Incidence p |  |
| Kaku, 2011[99](#_ENREF_99)  RCT | Grp1: Glibenclamide Fixed (1.25 -2.5 mg/d) Grp2: Liraglutide Titrated (Max: 0.9 mg/d) ITT: No Followup (wks): 26 |  |  | Def:CVD morbidity CVD morbidity composite outcome (see comments) Incidence p  Incidence p |  |
| Kaku, 2011[99](#_ENREF_99)  RCT | Grp1: Glibenclamide Fixed (1.25 -2.5 mg/d) Grp2: Liraglutide Titrated (Max: 0.9 mg/d) ITT: No Followup (wks): 26 |  |  | Def:CVD morbidity CVD morbidity composite outcome (see comments) Incidence p  Incidence p |  |
| Kvapil, 2006[105](#_ENREF_105)  RCT | Grp1: Metformin + sulfonylurea  Fixed; Varied  Start: 1660 mg; Start: 1.75 mg, Max: 10.5, Mean: 6.58  Grp2: Metformin + aspart 70/30  Fixed; Varied  Start: 1660 mg; Start: 0.2 U/kg BID, Mean: 0.3 BID | Grp1: 0 (0)  Grp2: 1 | Def: Fatal MI  Grp1: 0 (0)  Grp2: 1 |  |  |
| Lavalle-Gonzalez, 2013[106](#_ENREF_106)  RCT | Grp1: Metformin + placebo Fixed ((ΓëÑ2,000 mg/day [or ΓëÑ1,500 mg/day if unable to tolerate higher dose])) Grp2: Metformin + sitagliptin Fixed ((ΓëÑ2,000 mg/day [or ΓëÑ1,500 mg/day if unable to tolerate higher dose])) Fixed (100mg) ITT: Yes Followup (wks): 52  Active |  |  | Def:CVD morbidity Nonfatal MI (not specified) Incidence Grp1: 1    Incidence Grp2: 0 |  |
| Lavalle-Gonzalez, 2013[106](#_ENREF_106)  RCT | Grp1: Metformin + placebo Fixed ((ΓëÑ2,000 mg/day [or ΓëÑ1,500 mg/day if unable to tolerate higher dose])) Grp2: Metformin + canagliflozin Fixed ((ΓëÑ2,000 mg/day [or ΓëÑ1,500 mg/day if unable to tolerate higher dose])) Fixed (100mg) ITT: Yes Followup (wks): 104 |  |  | Def:CVD morbidity Nonfatal MI (not defined) Incidence Grp1: 10   NA p NR RR  Incidence Grp2: 6   NA p NR RR 0.6 |  |
| Lavalle-Gonzalez, 2013[106](#_ENREF_106)  RCT | Grp1: Metformin + placebo Fixed ((ΓëÑ2,000 mg/day [or ΓëÑ1,500 mg/day if unable to tolerate higher dose]))    Grp2: Metformin + canagliflozin Fixed ((ΓëÑ2,000 mg/day [or ΓëÑ1,500 mg/day if unable to tolerate higher dose])) Fixed (300mg) ITT: Yes Followup (wks): 104 |  |  | Def:CVD morbidity CVD morbidity composite outcome (Must have one of following: cardiovascular death, myocardial infarction, stroke, admission to hospital due to unstable angina) Incidence Grp1: 26   NA p NR RR  Incidence Grp2: 12   NA p NR RR 0.46 |  |
| Lavalle-Gonzalez, 2013[106](#_ENREF_106)  RCT | Grp1: Metformin + sitagliptin Fixed ((ΓëÑ2,000 mg/day [or ΓëÑ1,500 mg/day if unable to tolerate higher dose])) Fixed (100mg) Grp2: Metformin + canagliflozin Fixed ((ΓëÑ2,000 mg/day [or ΓëÑ1,500 mg/day if unable to tolerate higher dose])) Fixed (100mg) ITT: Yes Followup (wks): 104 |  |  | Def:CVD morbidity Other CVD morbidity (Admission to hospital due to unstable angina) Incidence Grp1: 3   NA p NR RR  Incidence Grp2: 3   NA p NR RR 1 |  |
| Lavalle-Gonzalez, 2013[106](#_ENREF_106)  RCT | Grp1: Metformin + sitagliptin Fixed ((ΓëÑ2,000 mg/day [or ΓëÑ1,500 mg/day if unable to tolerate higher dose])) Fixed (100mg) Grp2: Metformin + canagliflozin Fixed ((ΓëÑ2,000 mg/day [or ΓëÑ1,500 mg/day if unable to tolerate higher dose])) Fixed (300mg) ITT: No Followup (wks): 50 |  |  | Def:CVD morbidity Other CVD morbidity (acute MI) Incidence Grp1:    Incidence Grp2: |  |
| Lawrence, 2004[107](#_ENREF_107)  RCT | Grp1: Metformin  Varied  Start: 500 mg bid, Max: 1000 mg tid  Grp2: Pioglitazone  Varied  Start: 30 mg, Max: 45 mg | Grp1: 1 (5)  Grp2: 0 (0) | Def: CVD mortality/Fatal MI  Grp1: 1 (5)  Grp2: 0 (0) | Def: CVD morbidity/MI (non-fatal)  Grp1: 0 (0)  Grp2: 0 (0) |  |
| List, 2009[109](#_ENREF_109)  RCT | Grp1: Metformin Titrated (Max: 1500 mg/d) Grp2: Dapagliflozin Fixed (5mg) ITT: Yes Followup (wks): 12  Active |  |  | Def:CVD morbidity Unspecified CVD morbidity outcomeincreased blood glucose Incidence Grp1: 0    Incidence Grp2: 0 |  |
| List, 2009[109](#_ENREF_109)  RCT | Grp1: Metformin Titrated (Max: 1500 mg/d) Grp2: Dapagliflozin Fixed (10 mg) ITT: Yes Followup (wks): 12  Active |  |  | Def:CVD morbidity Unspecified CVD morbidity outcomeincreased blood glucose Incidence Grp1: 0    Incidence Grp2: 0 |  |
| Malone, 2003[112](#_ENREF_112)  RCT | Grp1: Metformin + glibenclamide  Varied; Varied, fasting and pre-meal goal <7mmol/L, 2-hour post-prandial goal <10mmol/L  Max: 2550 mg, Mean: 1968 mg; Mean: 14.2 mg  D: 4 wks; 16 wks  Grp2: Metformin + lispro 75/25  Varied; Varied, fasting and pre-meal goal <7mmol/L, 2-hour post-prandial goal <10mmol/L  Max: 2550 mg; Mean: 0.19 U/kg in am and 0.14 U/kg in evening  D: 4 wks; 16 wks | Grp1: 0 (0)  Grp2: 1 (<1) |  |  |  |
| Malone, 2005[205](#_ENREF_205)  RCT | Grp1: Metformin + lispro 75/25  Varied, pre-meal glucose 90-126 mg/dL; 2-hr postprandial 144-180 mg/dL  Start: 1500 mg, Max: 2550 mg, Mean: 2146 mg; Mean: 0.42 U/kg BID  D: 4 wks, 16 wks  Grp2: Metformin + glargine  Varied, pre-meal glucose 90-126 mg/dL  Start: 1500 mg, Max: 2500 mg, Mean: 2146 mg; Mean: 0.36 U/Kg QD  D: 4 wks, 16 wks | Grp1: 1 (2)  Grp2: 1 (2) | Grp1: 1 (2)  Grp2: 0 (0) |  |  |
| Masica, 2013[206](#_ENREF_206)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: TZD Not specified   ITT: Yes Followup (wks): 12  Active |  |  | Def:CVD morbidity Unspecified CVD morbidity outcomeincreased blood glucose Incidence Grp1: 0    Incidence Grp2: 0 |  |
| Masica, 2013[206](#_ENREF_206)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: TZD Not specified   ITT: Yes Followup (wks): 26  Passive |  |  | Def:CVD morbidity Other CVD morbidity (discontinuation due to hypertensive heart disease. Discontinuation because of serious adverse event.) Incidence Grp1:    Incidence Grp2: |  |
| Masica, 2013[206](#_ENREF_206)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 26  Passive |  |  | Def:CVD morbidity Other CVD morbidity (discontinuation due to hypertensive heart disease. Discontinuation because of serious adverse event.) Incidence Grp1:    Incidence Grp2: 1 |  |
| Masica, 2013[206](#_ENREF_206)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 12 |  |  | Def:CVD morbidity Other CVD morbidity (CEC-confirmed cardiovascular event - ST elevation myocardial infarction) Incidence Grp1:    Incidence Grp2: 1 |  |
| Masica, 2013[206](#_ENREF_206)  Retrospective cohort | Grp1: SU Not specified   Grp2: TZD Not specified   ITT: Yes Followup (wks): 12 |  |  | Def:CVD morbidity Other CVD morbidity (acute MI) Incidence Grp1: 0    Incidence Grp2: 2 |  |
| Masica, 2013[206](#_ENREF_206)  Retrospective cohort | Grp1: SU Not specified   Grp2: TZD Not specified   ITT: No Followup (wks): 12  NR/unclear |  |  | Def:CVD morbidity Other CVD morbidity (Prinzmetal angina) Incidence Grp1: 1    Incidence Grp2: |  |
| Mogensen, 2014[207](#_ENREF_207)  Retrospective cohort | Grp1: Metformin + glp-1 agonist Not specified   Not specified   Grp2: Metformin + basal insulin Not specified   Not specified   ITT: No Followup (wks): 12  NR/unclear |  |  | Def:CVD morbidity Other CVD morbidity (Prinzmetal angina) Incidence Grp1: 1    Incidence Grp2: |  |
| Mogensen, 2014[207](#_ENREF_207)  Retrospective cohort | Grp1: Metformin + glp-1 agonist Not specified   Not specified   Grp2: Metformin + basal insulin Not specified   Not specified   ITT: No Followup (wks): 48 |  |  | Def:CVD morbidity Nonfatal MI (no definition) Incidence Grp1: 0    Incidence Grp2: 0 |  |
| Mogensen, 2014[207](#_ENREF_207)  Retrospective cohort | Grp1: Metformin + su Not specified   Not specified   Grp2: Metformin + glp-1 agonist Not specified   Not specified   ITT: Yes Followup (wks):   Active |  |  | Def:CVD morbidity Nonfatal MI (non ST segment myocardial infarction with pulmonary edema and stent placed) Incidence Grp1:    Incidence Grp2: 1 |  |
| Mogensen, 2014[207](#_ENREF_207)  Retrospective cohort | Grp1: Metformin + su Not specified   Not specified   Grp2: Metformin + glp-1 agonist Not specified   Not specified   ITT: Not applicable (e.g., cohort) Followup (wks): |  |  | Def:CVD morbidity CVD morbidity composite outcome (ICD9 410-413, 414-414.05, 414.8, 414.9, 428.9, 430-438, 440-448 (Except 440 and 440.1)) Incidence Grp1:  2241 Person-years p NR RH 0.31 Incidence Grp2:  1017 Person-years p NR RH ref |  |
| Mogensen, 2014[207](#_ENREF_207)  Retrospective cohort | Grp1: Metformin + su Not specified   Not specified   Grp2: Metformin + dpp-4 inhibitor Not specified   Not specified   ITT: Not applicable (e.g., cohort) Followup (wks): |  |  | Def:CVD morbidity CVD morbidity composite outcome (ICD9 410-413, 414-414.05, 414.8, 414.9, 428.9, 430-438, 440-448 (Except 440 and 440.1)) Incidence Grp1:  2241 Person-years p NR RH 0.31 Incidence Grp2:  745 Person-years p NR RH 0.52 |  |
| Mogensen, 2014[207](#_ENREF_207)  Retrospective cohort | Grp1: Metformin + su Not specified   Not specified   Grp2: Metformin + dpp-4 inhibitor Not specified   Not specified   ITT: Yes Followup (wks): 16  NR/unclear |  |  | Def:CVD morbidity Nonfatal MI (Discontinuation due to myocardial ischemia - did not specify as fatal or nonfatal) Incidence Grp1: 1    Incidence Grp2: |  |
| Mogensen, 2014[207](#_ENREF_207)  Retrospective cohort | Grp1: Metformin + su Not specified   Not specified   Grp2: Metformin + basal insulin Not specified   Not specified   ITT: No Followup (wks): 58 |  |  | Def:CVD morbidity CVD morbidity composite outcome (vascular events) Incidence Grp1: 11    Incidence Grp2: 8 |  |
| Mogensen, 2014[207](#_ENREF_207)  Retrospective cohort | Grp1: Metformin + su Not specified   Not specified   Grp2: Metformin + basal insulin Not specified   Not specified   ITT: No Followup (wks): 58 |  |  | Def:CVD morbidity CVD morbidity composite outcome (vascular event) Incidence Grp1:  100 Person-years p NR  Incidence Grp2:  100 Person-years p NR |  |
| Mogensen, 2014[207](#_ENREF_207)  Retrospective cohort | Grp1: Metformin + dpp-4 inhibitor Not specified   Not specified   Grp2: Metformin + glp-1 agonist Not specified   Not specified   ITT: Yes Followup (wks): 144 |  |  | Def:CVD morbidity CVD morbidity composite outcome (including nonfatal myocardial infarction, nonfatal stroke, or arterial revascularization by PTCA or by coronary artery bypass graft, death from a cardiovascular cause, and death from any cause, obtained and confirmed by th Incidence Grp1: 39   NA p NR RH 0.54 Incidence Grp2: 52   NA p NR RH |  |
| Mogensen, 2014[207](#_ENREF_207)  Retrospective cohort | Grp1: Metformin + dpp-4 inhibitor Not specified   Not specified   Grp2: Metformin + glp-1 agonist Not specified   Not specified   ITT: Yes Followup (wks): 144  Active |  |  | Def:CVD morbidity Other CVD morbidity (new peripheral vascular disease events not further specified but confirmed by medical record) Incidence Grp1: 1   NA p NR RH 0.13 Incidence Grp2: 6   NA p NR RH |  |
| Mogensen, 2014[207](#_ENREF_207)  Retrospective cohort | Grp1: Metformin + dpp-4 inhibitor Not specified   Not specified   Grp2: Metformin + basal insulin Not specified   Not specified   ITT: Yes Followup (wks): 144 |  |  | Def:CVD morbidity Other CVD morbidity (new or worsening angina confirmed by medical record) Incidence Grp1: 77   NA p NR RH 1.07 Incidence Grp2: 71   NA p NR RH |  |
| Mogensen, 2014[207](#_ENREF_207)  Retrospective cohort | Grp1: Metformin + dpp-4 inhibitor Not specified   Not specified   Grp2: Metformin + basal insulin Not specified   Not specified   ITT: Yes Followup (wks): 144 |  |  | Def:CVD morbidity Other CVD morbidity (new critical cardiac arrhythmia confirmed by medical record) Incidence Grp1: 30   NA p NR RH 1.01 Incidence Grp2: 27   NA p NR RH |  |
| Nauck, 2007[118](#_ENREF_118)  RCT | Grp1: Metformin + glipizide  NR  Grp2: Metformin + sitagliptin  NR | Grp1: 2 (0.3)  Grp2: 1 (0.2) | Def: Fatal MI  Grp1: 1 (0.2)  Grp2: 0 (0) |  |  |
| Nauck, 2009[119](#_ENREF_119)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1868mg>=1500mg or maximum tolerated dose) Grp2: Metformin + alogliptin Fixed (Mean: 1846mg>=1500mg or maximum tolerated dose) Fixed (25mg) ITT: Yes Followup (wks): 144 |  |  | Def:CVD morbidity Nonfatal MI (no specific definition - confirmed by medical records at each institution) Incidence Grp1: 5    Incidence Grp2: 6 |  |
| Nauck, 2009[119](#_ENREF_119)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1868mg>=1500mg or maximum tolerated dose) Grp2: Metformin + alogliptin Fixed (Mean: 1837mg>=1500mg or maximum tolerated dose) Fixed (12.5mg) ITT: Yes Followup (wks): 144 |  |  | Def:CVD morbidity Other CVD morbidity (arterial revascularization by PTCA or by coronary artery bypass graft confirmed by medical records) Incidence Grp1: 21    Incidence Grp2: 25 |  |
| Nauck, 2009[119](#_ENREF_119)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1868mg>=1500mg or maximum tolerated dose)    Grp2: Metformin + alogliptin Fixed (Mean: 1846mg>=1500mg or maximum tolerated dose) Fixed (25mg) ITT: Not applicable (e.g., cohort) Followup (wks): 260 |  |  | Def:CVD morbidity CVD morbidity composite outcome (AMI and stroke events only) Incidence Grp1:  179351 Person-years p NR RH 1.00 (ref) Incidence Grp2:  101125 Person-years p NR RH 1.15 |  |
| Nauck, 2009[119](#_ENREF_119)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1868mg>=1500mg or maximum tolerated dose) Grp2: Metformin + alogliptin Fixed (Mean: 1837mg>=1500mg or maximum tolerated dose) Fixed (12.5mg) ITT: Not applicable (e.g., cohort) Followup (wks): 260 |  |  | Def:CVD morbidity CVD morbidity composite outcome (hospitalization for acute myocardial infarction (AMI) or stroke, or death) Incidence Grp1:  179351 Person-years p NR RH 1.00 (Ref) Incidence Grp2:  101125 Person-years p NR RH 1.21 |  |
| Nauck, 2009[119](#_ENREF_119)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1868mg>=1500mg or maximum tolerated dose) Grp2: Metformin + alogliptin Fixed (Mean: 1846mg>=1500mg or maximum tolerated dose) Fixed (25mg) ITT: Not applicable (e.g., cohort) Followup (wks): |  |  | Def:CVD morbidity CVD morbidity composite outcome (hospitalization for acute myocardial infarction (AMI) or stroke, or death) Incidence p RH 1 Incidence p RH 1.18 |  |
| Nauck, 2009[119](#_ENREF_119)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1868mg>=1500mg or maximum tolerated dose) Grp2: Metformin + alogliptin Fixed (Mean: 1837mg>=1500mg or maximum tolerated dose) Fixed (12.5mg) ITT: Not applicable (e.g., cohort) Followup (wks): |  |  | Def:CVD morbidity CVD morbidity composite outcome (hospitalization for acute myocardial infarction (AMI) or stroke, or death) Incidence p RH 1 Incidence p RH 1.28 |  |
| Nauck, 2011[120](#_ENREF_120)  RCT | Grp1: Metformin + glipizide Fixed (1500 - 2500 mg) Titrated (Mean: 16.4 mgMax: 20 mg) Grp2: Metformin + dapagliflozin Fixed (1500 - 2500 mg) Titrated (Mean: 9.2 mgMax: 10 mg) ITT: Not applicable (e.g., cohort) Followup (wks): |  |  | Def:CVD morbidity Other CVD morbidity Incidence p RH 1 Incidence p RH 1.24 |  |
| Nauck, 2011[120](#_ENREF_120)  RCT | Grp1: Metformin + glipizide Fixed (1500 - 2500 mg) Titrated (Mean: 16.4 mgMax: 20 mg) Grp2: Metformin + dapagliflozin Fixed (1500 - 2500 mg) Titrated (Mean: 9.2 mgMax: 10 mg) ITT: Not applicable (e.g., cohort) Followup (wks): |  |  | Def:CVD morbidity CVD morbidity composite outcome (hospitalization for acute myocardial infarction (AMI) or stroke, or death) Incidence p RH 1 Incidence p RH 1.18 |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + placebo Fixed (>=1500 mg/day) Grp2: Metformin + sitagliptin Fixed (>=1500 mg/day) Fixed (100 mg) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  |  | Def:CVD morbidity CVD morbidity composite outcome (diagnosis of myocardial infarction, angina pectoris, intracerebral haemorrhage, cerebral infarction, unspecified stroke, peripheral vascular disease, or intervention with percutaneous coronary intervention or coronary arte Incidence Grp1: 1734   p RH 1.00 REF Incidence Grp2: 1338   p RH 1.28 |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + placebo Fixed (>=1500 mg/day) Grp2: Metformin + sitagliptin Fixed (>=1500 mg/day) Fixed (100 mg) ITT: No Followup (wks): 25  NR/unclear |  |  | Def:CVD morbidity Other CVD morbidity (UNstable angina) Incidence Grp1: 0   p NR  Incidence Grp2: 2   p NR |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + placebo Fixed (>=1500 mg/day) Grp2: Metformin + sitagliptin Fixed (>=1500 mg/day) Fixed (100 mg) ITT: No Followup (wks): 25  NR/unclear |  |  | Def:CVD morbidity Other CVD morbidity (carotid artery occlusion) Incidence Grp1: 0   p  Incidence Grp2: 1   p |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + placebo Fixed (>=1500 mg/day) Grp2: Metformin + dulaglutide Fixed (>=1500 mg/day) Fixed (0.75 mg/week) ITT: No Followup (wks): 25  NR/unclear |  |  | Def:CVD morbidity Nonfatal MI (Acute myocardial infarction) Incidence Grp1: 1    Incidence Grp2: 0 |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + placebo Fixed (>=1500 mg/day) Grp2: Metformin + dulaglutide Fixed (>=1500 mg/day) Fixed (0.75 mg/week) ITT:  Followup (wks): 25  NR/unclear |  |  | Def:CVD morbidity Other CVD morbidity (Angina pectoris) Incidence Grp1: 1   Persons p NR  Incidence Grp2: 1   Persons p NR |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + placebo Fixed (>=1500 mg/day) Grp2: Metformin + dulaglutide Fixed (>=1500 mg/day) Fixed (1.5 mg/week) ITT: No Followup (wks): 18  NR/unclear |  |  | Def:CVD morbidity Nonfatal MI (Acute cardiovascular event- Myocardial ischemia or MI) Incidence Grp1: 1   Persons p  Incidence Grp2: 1   Persons p |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + placebo Fixed (>=1500 mg/day) Grp2: Metformin + dulaglutide Fixed (>=1500 mg/day) Fixed (1.5 mg/week) ITT: No Followup (wks): 52  NR/unclear |  |  | Def:CVD morbidity Other CVD morbidity (Vascular Disorders') Incidence Grp1: 10 (7.6) p  Incidence Grp2: 17 (6.3) p |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + placebo Fixed (>=1500 mg/day) Grp2: Metformin + dulaglutide Fixed (>=1500 mg/day) Fixed (0.75 mg/week) ITT: No Followup (wks): 52  NR/unclear |  |  | Def:CVD morbidity Other CVD morbidity (Cardiac disorders') Incidence Grp1: 14 (10.6) NA p  Incidence Grp2: 17 (6.3) NA p |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + placebo Fixed (>=1500 mg/day) Grp2: Metformin + dulaglutide Fixed (>=1500 mg/day) Fixed (1.5 mg/week) ITT: Yes Followup (wks): 24 |  |  | Def:CVD morbidity Other CVD morbidity (defined as 'acute cardiovascuar event') Incidence Grp1: 1   p  Incidence Grp2: 1   p |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + sitagliptin Fixed (>=1500 mg/day) Fixed (100 mg) Grp2: Metformin + dulaglutide Fixed (>=1500 mg/day) Fixed (0.75 mg/week) ITT: No Followup (wks): 80  NR/unclear |  |  | Def:CVD morbidity CVD morbidity composite outcome (ischemic events') Incidence Grp1: 4 (1) p  Incidence Grp2: 6 (2) p |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + sitagliptin Fixed (>=1500 mg/day) Fixed (100 mg) Grp2: Metformin + dulaglutide Fixed (>=1500 mg/day) Fixed (0.75 mg/week) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  |  | Def:CVD morbidity CVD morbidity composite outcome (MI, Stroke and CV death based on ICD-10 codes composite of MI (I21â€“I22), stroke (I61â€“I64) cardiovascular death (I00 â€“I99)) Incidence Grp1: 1646   p RH 1 Incidence Grp2: 1376   p RH 1.12 |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + sitagliptin Fixed (>=1500 mg/day) Fixed (100 mg) Grp2: Metformin + dulaglutide Fixed (>=1500 mg/day) Fixed (1.5 mg/week) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  |  | Def:CVD morbidity CVD morbidity composite outcome (MI, Stroke and CV death based on ICD-10 codes composite of MI (I21â€“I22), stroke (I61â€“I64) cardiovascular death (I00 â€“I99)) Incidence Grp1: 245   p RH 1 Incidence Grp2: 267   p RH 1.29 |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + sitagliptin Fixed (>=1500 mg/day) Fixed (100 mg) Grp2: Metformin + dulaglutide Fixed (>=1500 mg/day) Fixed (1.5 mg/week) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  |  | Def:CVD morbidity CVD morbidity composite outcome (MI, Stroke and CV death based on ICD-10 codes composite of MI (I21â€“I22), stroke (I61â€“I64) cardiovascular death (I00 â€“I99)) Incidence Grp1: 1646   p RH 1 Incidence Grp2: 820   p RH 1.17 |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + sitagliptin Fixed (>=1500 mg/day) Fixed (100 mg) Grp2: Metformin + dulaglutide Fixed (>=1500 mg/day) Fixed (0.75 mg/week) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  |  | Def:CVD morbidity CVD morbidity composite outcome (MI, Stroke and CV death based on ICD-10 codes composite of MI (I21â€“I22), stroke (I61â€“I64) cardiovascular death (I00 â€“I99)) Incidence Grp1: 245   p RH 1 Incidence Grp2: 154   p RH 1.46 |  |
| Nauck, 2014[121](#_ENREF_121)  RCT | Grp1: Metformin + sitagliptin Fixed (>=1500 mg/day) Fixed (100 mg) Grp2: Metformin + dulaglutide Fixed (>=1500 mg/day) Fixed (1.5 mg/week) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  |  | Def:CVD morbidity CVD morbidity composite outcome (MI, Stroke and CV death based on ICD-10 codes composite of MI (I21â€“I22), stroke (I61â€“I64) cardiovascular death (I00 â€“I99)) Incidence Grp1: 245   p RH 1 Incidence Grp2: 751   p RH 1.29 |  |
| Pantalone, 2009[208](#_ENREF_208)  Cohort | Grp1: Metformin  NR  Grp2: Rosiglitazone  NR | Grp1: ref  Grp2: HR: 1.33 (CI: 0.93 to 1.91) p: 0.11 |  | Def: CABG, PTCA, MI, or diagnosis of CAD by ICD-9 after baseline  Grp1: ref  Grp2: HR: 0.96 (CI: 0.76 to 1.21) p: 0.74 |  |
| Pantalone, 2009[208](#_ENREF_208)  Cohort | Grp1: Metformin  NR  Grp2: Pioglitazone  NR | Grp1: ref  Grp2: HR: 1.08 (CI: 0.78 to 1.51) p: 0.64 |  | Def: CABG, PTCA, MI, or diagnosis of CAD by ICD-9 after baseline  Grp1: ref  Grp2: HR: 1.11 (CI: 0.91 to 1.34) p: 0.32 |  |
| Pantalone, 2009[208](#_ENREF_208)  Cohort | Grp1: Metformin  NR  Grp2: Sulfonylurea  NR | Grp1: HR: 0.54 (CI: 0.46 to 0.64) p: <0.001  Grp2: ref |  | Def: CABG, PTCA, MI, or diagnosis of CAD by ICD-9 after baseline  Grp1: HR: 0.94 (CI: 0.85 to 1.05) p: 0.23  Grp2: ref |  |
| Pantalone, 2009[208](#_ENREF_208)  Cohort | Grp1: Rosiglitazone  NR  Grp2: Pioglitazone  NR | Grp1: ref  Grp2: HR: 0.81 (CI: 0.52 to 1.27) p: 0.36 |  | Def: CABG, PTCA, MI, or diagnosis of CAD by ICD-9 after baseline  Grp1: ref  Grp2: HR: 1.15 (CI: 0.87 to 1.53) p: 0.32 |  |
| Pantalone, 2009[208](#_ENREF_208)  Cohort | Grp1: Rosiglitazone  NR  Grp2: Sulfonylurea  NR | Grp1: HR: 0.73 (CI: 0.51 to 1.02) p: 0.08  Grp2: ref |  | Def: CABG, PTCA, MI, or diagnosis of CAD by ICD-9 after baseline  Grp1: HR: 0.90 (CI: 0.71 to 1.14) p: 0.41  Grp2: ref |  |
| Pantalone, 2009[208](#_ENREF_208)  Cohort | Grp1: Pioglitazone  NR  Grp2: Sulfonylurea  NR | Grp1: HR: 0.59 (CI: 0.43 to 0.81) p: <0.001  Grp2: ref |  | Def: CABG, PTCA, MI, or diagnosis of CAD by ICD-9 after baseline  Grp1: HR: 1.04 (CI: 0.86 to 1.26) p: 0.69  Grp2: ref |  |
| Pantalone, 2012[209](#_ENREF_209)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Glipizide Not specified   ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  |  | Def:CVD morbidity CVD morbidity composite outcome (MI, Stroke and CV death based on ICD-10 codes composite of MI (I21â€“I22), stroke (I61â€“I64) cardiovascular death (I00 â€“I99)) Incidence Grp1: 1646   p RH 1 Incidence Grp2: 3517   p RH 1.21 |  |
| Pantalone, 2012[209](#_ENREF_209)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Glyburide Not specified   ITT: No Followup (wks): 24 |  |  | Def:CVD morbidity CVD morbidity composite outcome (not prespecified as a composite outcome but this is what is reported on - CAD, carotid artery stenosis, peripheral artery disease) Incidence p  Incidence p |  |
| Pantalone, 2012[209](#_ENREF_209)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Glimepiride Not specified   ITT: Not applicable (e.g., cohort) Followup (wks): |  |  | Def:CVD morbidity Nonfatal MI (ï¬rst-time discharge diagnosis of MI) Incidence Grp1: 599  5927 Persons p OR 0.86 Incidence Grp2: 3080  26778 Persons p OR 1 REF |  |
| Petrica, 2009[126](#_ENREF_126)  RCT | Grp1: Metformin + rosiglitazone Fixed (1700 mg/day) Fixed (4 mg/day) Grp2: Metformin + glimepiride Fixed (1700 mg/day) Fixed (4 mg/day) ITT: Yes Followup (wks): 76  NR/unclear |  |  | Def:CVD morbidity Other CVD morbidity (acute CVD adverse events (unspecified)) Incidence Grp1: (2.1)  Incidence Grp2: |  |
| Petrica, 2009[126](#_ENREF_126)  RCT | Grp1: Metformin + rosiglitazone Fixed (1700 mg/day) Fixed (4 mg/day) Grp2: Metformin + glimepiride Fixed (1700 mg/day) Fixed (4 mg/day) ITT: Yes Followup (wks): 76  NR/unclear |  |  | Def:CVD morbidity Other CVD morbidity (acute CVD adverse events (unspecified)) Incidence Grp1: (2.1)  Incidence Grp2: (0.3) |  |
| Pfutzner, 2011[128](#_ENREF_128)  RCT | Grp1: Metformin + pioglitazone Fixed (1700 mg/d) Fixed (30 mg/d) Grp2: Metformin + glimepiride Fixed (1700 mg/d) Fixed (2mg/d) ITT: Yes Followup (wks): 76  NR/unclear |  |  | Def:CVD morbidity Other CVD morbidity (acute CVD adverse events (unspecified)) Incidence Grp1: (2.1)  Incidence Grp2: |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Metformin + placebo Titrated (Max: 2000 mg) Grp2: Saxagliptin + placebo Fixed (10 mg) ITT: Yes Followup (wks): 76  NR/unclear |  |  | Def:CVD morbidity Other CVD morbidity (acute CVD adverse events (unspecified)) Incidence Grp1:    Incidence Grp2: (0.3) |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Metformin + placebo Titrated (Max: 2000 mg) Grp2: Saxagliptin + placebo Fixed (10 mg) ITT: Yes Followup (wks): 76  NR/unclear |  |  | Def:CVD morbidity Other CVD morbidity (acute CVD adverse events (unspecified)) Incidence Grp1:    Incidence Grp2: |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Metformin + placebo Titrated (Max: 2000 mg) Grp2: Saxagliptin + placebo Fixed (10 mg) ITT: Yes Followup (wks): 104 |  |  | Def:CVD morbidity Nonfatal MI (myocardial infarction, judged to have a possible relationship to trial drug by investigator) Incidence Grp1: 1    Incidence Grp2: 1 |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Metformin + placebo Titrated (Max: 2000 mg) Grp2: Saxagliptin + placebo Fixed (10 mg) ITT:  Followup (wks): 104 |  |  | Def:CVD morbidity Other CVD morbidity (cardiac disorders) Incidence Grp1: 14 (6)  Incidence Grp2: 8 (3) |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Metformin + placebo Titrated (Max: 2000 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT:  Followup (wks): 104 |  |  | Def:CVD morbidity Other CVD morbidity (cardiac disorders) Incidence Grp1: 14 (6)  Incidence Grp2: 11 (5) |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Metformin + placebo Titrated (Max: 2000 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (10 mg) ITT: Yes Followup (wks): 104 |  |  | Def:CVD morbidity Nonfatal MI (myocardial infarction, judged to have a possible relationship to trial drug by investigator) Incidence Grp1: 1    Incidence Grp2: 1 |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Metformin + placebo Titrated (Max: 2000 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: Not applicable (e.g., cohort) Followup (wks): |  |  | Def:CVD morbidity CVD morbidity composite outcome (death from any cause or first hospitalization for myocardial infarction (ICD-9 code 410-412.99 and 414. xx), cerebrovascular disease (430â€“437.1 and procedure code 38.12), coronary artery bypass graft (36.10â€“36.16 and 3 Incidence p RH  Incidence p RH 1.15 |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Metformin + placebo Titrated (Max: 2000 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (10 mg) ITT: NR Followup (wks): 104 |  |  | Def:CVD morbidity CVD morbidity composite outcome (CV AEs (qualitatively reported)) Incidence p  Incidence p |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Metformin + placebo Titrated (Max: 2000 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: No Followup (wks): 26 |  |  | Def:CVD morbidity Other CVD morbidity (Unstable Angina) Incidence Grp1: 1 (1) Persons p  Incidence Grp2: 0 (0) Persons p |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Metformin + placebo Titrated (Max: 2000 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (10 mg) ITT: No Followup (wks): 26 |  |  | Def:CVD morbidity Other CVD morbidity (Coronary artery occlusion) Incidence Grp1: 2 (1) Persons p NR  Incidence Grp2: 0 (0) Persons p NR |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Metformin + placebo Titrated (Max: 2000 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: No Followup (wks): 26 |  |  | Def:CVD morbidity Other CVD morbidity (Unstable Angina) Incidence Grp1: 1 (1) Persons p  Incidence Grp2: 0 (0) Persons p |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Metformin + placebo Titrated (Max: 2000 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (10 mg) ITT: No Followup (wks): 26 |  |  | Def:CVD morbidity Other CVD morbidity (Coronary artery occlusion) Incidence Grp1: 2 (1) Persons p NR  Incidence Grp2: 0 (0) Persons p NR |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Saxagliptin + placebo Fixed (10 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: No Followup (wks): 26 |  |  | Def:CVD morbidity Other CVD morbidity (Unstable Angina) Incidence Grp1: 0 (0) Persons p  Incidence Grp2: 0 (0) Persons p |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Saxagliptin + placebo Fixed (10 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (10 mg) ITT: No Followup (wks): 26 |  |  | Def:CVD morbidity Other CVD morbidity (Coronary artery occlusion) Incidence Grp1: 0 (0) Persons p NR  Incidence Grp2: 0 (0) Persons p NR |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Saxagliptin + placebo Fixed (10 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: Not applicable (e.g., cohort) Followup (wks): |  |  | Def:CVD morbidity CVD morbidity composite outcome (all-cause mortality, AMI and stroke) Incidence Grp1: 4286 (5.1) p RR REF Incidence Grp2: 62 (5) p RR 1.22 |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Saxagliptin + placebo Fixed (10 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (10 mg) ITT: Yes Followup (wks): 102 |  | Def:CVD mortality Other CVD mortality (cardiopulmonary arrest and myocardial infarction) Incidence Grp1:    Incidence Grp2: 2 |  |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Saxagliptin + placebo Fixed (10 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 102 |  | Def:CVD mortality Other CVD mortality (cardiopulmonary arrest and myocardial infarction) Incidence Grp1:    Incidence Grp2: |  |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Saxagliptin + placebo Fixed (10 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (10 mg) ITT: Yes Followup (wks): 102 |  | Def:CVD mortality Other CVD mortality (cardiopulmonary arrest and myocardial infarction) Incidence Grp1:    Incidence Grp2: |  |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Saxagliptin + placebo Fixed (10 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (5 mg) ITT: Yes Followup (wks): 52  Active |  | Def:CVD mortality Fatal MI Incidence Grp1: 0    Incidence Grp2: 1 |  |  |
| Pfutzner, 2011[129](#_ENREF_129)  RCT | Grp1: Saxagliptin + placebo Fixed (10 mg) Grp2: Metformin + saxagliptin Titrated (Max: 2000 mg) Fixed (10 mg) ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Composite CVD mortality outcome (sudden cardiac death, fatal myocardial infarction, and fatal stroke) Incidence Grp1: 2   NA p NR RR  Incidence Grp2: 2   NA p NR RR 1 |  |  |
| Pratley, 2010[130](#_ENREF_130)  RCT | Grp1: Metformin + sitagliptin  NS; Max: 100 mg  Grp2: Metformin + liraglutide  Varied, HgbA1c: 7.5-10%  NS; Start: 0.6 mg, Max: 1.8 mg |  | Def: Fatal cardiac arrest  Grp1: 1 (<1)  Grp2: 0 (0) |  |  |
| Pratley, 2010[130](#_ENREF_130)  RCT | Grp1: Metformin + sitagliptin  NS; Max: 100 mg  Grp2: Metformin + liraglutide  Varied, HgbA1c: 7.5-10%  NS; Start: 0.6 mg, Max: 1.2 mg |  | Def: Fatal cardiac arrest  Grp1: 1 (<1)  Grp2: 0 (0) |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (2000 mg) Grp2: + alogliptin Fixed (25mg qd) ITT: No Followup (wks): 26  NR/unclear |  | Def:CVD mortality Other CVD mortality (sudden cardiac death) Incidence Grp1:    Incidence Grp2: |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: + alogliptin Fixed (25mg qd) ITT: No Followup (wks): 26  NR/unclear |  | Def:CVD mortality Other CVD mortality (sudden cardiac death) Incidence Grp1:    Incidence Grp2: |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (2000 mg) Grp2: + alogliptin Fixed (25mg qd) ITT: No Followup (wks): 26  NR/unclear |  | Def:CVD mortality Other CVD mortality (sudden cardiac death) Incidence Grp1:    Incidence Grp2: 1 |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: + alogliptin Fixed (25mg qd) ITT: No Followup (wks): 26  NR/unclear |  | Def:CVD mortality Other CVD mortality (sudden cardiac death) Incidence Grp1:    Incidence Grp2: |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: + alogliptin Fixed (25mg qd) ITT: No Followup (wks): 26  NR/unclear |  | Def:CVD mortality Other CVD mortality (sudden cardiac death) Incidence Grp1:    Incidence Grp2: |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (2000 mg) Grp2: + alogliptin Fixed (25mg qd) ITT: No Followup (wks): 26  NR/unclear |  | Def:CVD mortality Other CVD mortality (sudden cardiac death) Incidence Grp1:    Incidence Grp2: |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: Metformin + alogliptin Fixed (1000 mg) Fixed (25 mg) ITT: No Followup (wks): 26  NR/unclear |  | Def:CVD mortality Other CVD mortality (sudden cardiac death) Incidence Grp1: 1    Incidence Grp2: |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (2000 mg) Grp2: Metformin + alogliptin Fixed (1000 mg) Fixed (25 mg) ITT: No Followup (wks): 26  NR/unclear |  | Def:CVD mortality Other CVD mortality (sudden cardiac death) Incidence Grp1:    Incidence Grp2: |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: Metformin + alogliptin Fixed (2000 mg) Fixed (25 mg) ITT: No Followup (wks): 26  NR/unclear |  | Def:CVD mortality Other CVD mortality (sudden cardiac death) Incidence Grp1:    Incidence Grp2: |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (2000 mg) Grp2: Metformin + alogliptin Fixed (2000 mg) Fixed (25 mg) ITT: No Followup (wks): 26  NR/unclear |  | Def:CVD mortality Other CVD mortality (sudden cardiac death) Incidence Grp1: 1    Incidence Grp2: |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (2000 mg) Grp2: Metformin + alogliptin Fixed (1000 mg) Fixed (25 mg) ITT: No Followup (wks): 26  NR/unclear |  | Def:CVD mortality Other CVD mortality (sudden cardiac death) Incidence Grp1:    Incidence Grp2: |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: Metformin + alogliptin Fixed (1000 mg) Fixed (25 mg) ITT: Yes Followup (wks): 24 |  | Def:CVD mortality Fatal MI Incidence Grp1: 0    Incidence Grp2: 0 |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (2000 mg) Grp2: Metformin + alogliptin Fixed (2000 mg) Fixed (25 mg) ITT: Yes Followup (wks): 24 |  | Def:CVD mortality Fatal MI Incidence Grp1: 1    Incidence Grp2: 0 |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: Metformin + alogliptin Fixed (2000 mg) Fixed (25 mg) ITT: Yes Followup (wks): 24 |  | Def:CVD mortality Fatal MI Incidence Grp1: 1    Incidence Grp2: 0 |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (2000 mg) Grp2: Metformin + alogliptin Fixed (1000 mg) Fixed (25 mg) ITT: Yes Followup (wks): 24 |  | Def:CVD mortality Fatal MI Incidence Grp1: 0    Incidence Grp2: 0 |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: Metformin + alogliptin Fixed (1000 mg) Fixed (25 mg) ITT: Yes Followup (wks): 24 |  | Def:CVD mortality Fatal MI Incidence Grp1: 0    Incidence Grp2: 0 |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (2000 mg) Grp2: Metformin + alogliptin Fixed (2000 mg) Fixed (25 mg) ITT: Yes Followup (wks): 24 |  | Def:CVD mortality Fatal MI Incidence Grp1: 1    Incidence Grp2: 0 |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin Fixed (1000 mg) Grp2: Metformin + alogliptin Fixed (2000 mg) Fixed (25 mg) ITT: Yes Followup (wks): 24 |  | Def:CVD mortality Fatal MI Incidence Grp1: 0    Incidence Grp2: 0 |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin + alogliptin Fixed (2000 mg) Fixed (25 mg) Grp2: + alogliptin Fixed (25mg qd) ITT: Yes Followup (wks): 24 |  | Def:CVD mortality Fatal MI Incidence Grp1: 0    Incidence Grp2: 0 |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin + alogliptin Fixed (1000 mg) Fixed (25 mg) Grp2: + alogliptin Fixed (25mg qd) ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Fatal MI Incidence Grp1: 1  408 Persons p NR  Incidence Grp2: 0  406 Persons p NR |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin + alogliptin Fixed (2000 mg) Fixed (25 mg) Grp2: + alogliptin Fixed (25mg qd) ITT: Yes Followup (wks): 12 |  | Def:CVD mortality Other CVD mortality (no fatal adverse events were reported) Incidence Grp1: 0    Incidence Grp2: 0 |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin + alogliptin Fixed (1000 mg) Fixed (25 mg) Grp2: + alogliptin Fixed (25mg qd) ITT: Not applicable (e.g., cohort) Followup (wks): |  | Def:CVD mortality Other CVD mortality (ICD-10: I00-I99) Incidence Grp1: 10  3246 Person-years p Rate ratio (poisson) 0.89 Incidence Grp2: 91  6916 Person-years p Rate ratio (poisson) 1.57 |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin + alogliptin Fixed (1000 mg) Fixed (25 mg) Grp2: + alogliptin Fixed (25mg qd) ITT: Not applicable (e.g., cohort) Followup (wks): |  | Def:CVD mortality Other CVD mortality (ICD-10: I00-I99) Incidence Grp1: 256  31497 Person-years p Rate ratio (poisson) 1 (Ref) Incidence Grp2: 10  3246 Person-years p Rate ratio (poisson) 0.89 |  |  |
| Pratley, 2014[131](#_ENREF_131)  RCT | Grp1: Metformin + alogliptin Fixed (2000 mg) Fixed (25 mg) Grp2: + alogliptin    Fixed (25mg qd) ITT: Not applicable (e.g., cohort) Followup (wks): |  | Def:CVD mortality Other CVD mortality (ICD-10: I00-I99) Incidence Grp1: 256  31497 Person-years p Rate ratio (poisson) 1 (Ref) Incidence Grp2: 38  11619 Person-years p Rate ratio (poisson) 0.57 |  |  |
| Qiu, 2014[132](#_ENREF_132)  RCT | Grp1: Metformin + placebo Fixed (Mean: 2131mg>= 2000mg/day,or >= 1500mg/day ifunable to tolerate a higher dose) for >=8 wks prior to screening) Grp2: Metformin + canagliflozin Fixed (Mean: 2137mg>= 2000mg/day,or >= 1500mg/dayifunable to tolerate a higher dose) for >= 8 wks prior to screening) Fixed (50mg BID) ITT: Not applicable (e.g., cohort) Followup (wks): |  | Def:CVD mortality Other CVD mortality (ICD-10: I00-I99) Incidence Grp1: 256  31497 Person-years p Rate ratio (poisson) 1 (Ref) Incidence Grp2: 91  6916 Person-years p Rate ratio (poisson) 1.57 |  |  |
| Qiu, 2014[132](#_ENREF_132)  RCT | Grp1: Metformin + placebo Fixed (Mean: 2131mg>= 2000mg/day,or >= 1500mg/day ifunable to tolerate a higher dose) for >=8 wks prior to screening) Grp2: Metformin + canagliflozin Fixed (Mean: 2128mg>= 2000mg/day,or >= 1500mg/dayifunable to tolerate a higher dose) for >= 8 wks prior to screening) Fixed (150mg BID) ITT: Not applicable (e.g., cohort) Followup (wks): |  | Def:CVD mortality Other CVD mortality (ICD-10: I00-I99) Incidence Grp1: 38  11619 Person-years p Rate ratio (poisson) 0.57 Incidence Grp2: 10  3246 Person-years p Rate ratio (poisson) 0.89 |  |  |
| Qiu, 2014[132](#_ENREF_132)  RCT | Grp1: Metformin + placebo Fixed (Mean: 2131mg>= 2000mg/day,or >= 1500mg/day ifunable to tolerate a higher dose) for >=8 wks prior to screening) Grp2: Metformin + canagliflozin Fixed (Mean: 2137mg>= 2000mg/day,or >= 1500mg/dayifunable to tolerate a higher dose) for >= 8 wks prior to screening) Fixed (50mg BID) ITT: Not applicable (e.g., cohort) Followup (wks): |  | Def:CVD mortality Other CVD mortality (ICD-10: I00-I99) Incidence Grp1: 38  11619 Person-years p Rate ratio (poisson) 0.57 Incidence Grp2: 91  6916 Person-years p Rate ratio (poisson) 1.57 |  |  |
| Qiu, 2014[132](#_ENREF_132)  RCT | Grp1: Metformin + placebo Fixed (Mean: 2131mg>= 2000mg/day,or >= 1500mg/day ifunable to tolerate a higher dose) for >=8 wks prior to screening) Grp2: Metformin + canagliflozin Fixed (Mean: 2128mg>= 2000mg/day,or >= 1500mg/dayifunable to tolerate a higher dose) for >= 8 wks prior to screening) Fixed (150mg BID) ITT: No Followup (wks): 48 |  | Def:CVD mortality Unspecified CVD mortality Incidence Grp1: 0    Incidence Grp2: 0 |  |  |
| Raz, 2008[188](#_ENREF_188)  RCT | Grp1: Metformin  Fixed  Grp2: Metformin + sitagliptin  Fixed  Max: 2550 mg; Mean: 100 mg | Grp1: 1 (1)  Grp2: 0 (0) | Def: Fatal MI  Grp1: 1 (1)  Grp2: 0 (0) |  |  |
| Reasner, 2011[135](#_ENREF_135)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + sitagliptin Titrated (Max: 2000 mg) Titrated (Max: 100 mg) ITT: No Followup (wks): 58 |  | Def:CVD mortality Fatal MI Incidence Grp1: 2    Incidence Grp2: |  |  |
| Reasner, 2011[135](#_ENREF_135)  RCT | Grp1: Metformin Titrated (Max: 2000 mg) Grp2: Metformin + sitagliptin Titrated (Max: 2000 mg) Titrated (Max: 100 mg) ITT: Yes Followup (wks): 144 |  | Def:CVD mortality Other CVD mortality (not specified but confirmed by medical record and death certificates at each institution) Incidence Grp1: 7    Incidence Grp2: 11 |  |  |
| Ridderstrale, 2014[136](#_ENREF_136)  RCT | Grp1: Metformin + glimepiride Fixed (Mean: 2.71 mg/day (mean max titrated dose of glimep(ΓëÑ1500 mg/day, maximum tolerated dose, or maximum dose according to the local label) Titrated (Max: 4mg) Grp2: Metformin + empagliflozin Fixed ((ΓëÑ1500 mg/day, maximum tolerated dose, or maximum dose according to the local label) Fixed (25mg) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  | Def:CVD mortality Composite CVD mortality outcome (death within 28 days of CVD was defined as diagnosis of myocardial infarction (ICD â€ 10 code I21), angina pectoris (ICD â€ 10 code I20.0), intracerebral haemorrhage, cerebral infarction, unspecified stroke (ICD â€ 10 c Incidence Grp1: 264   NA p NR RH 1.00 REF Incidence Grp2: 276   NA p NR RH Non-Proportional hazard, excluded from analysis |  |  |
| Ridderstrale, 2014[136](#_ENREF_136)  RCT | Grp1: Metformin + glimepiride Fixed (Mean: 2.71 mg/day (mean max titrated dose of glimep(ΓëÑ1500 mg/day, maximum tolerated dose, or maximum dose according to the local label) Titrated (Max: 4mg) Grp2: Metformin + empagliflozin Fixed ((ΓëÑ1500 mg/day, maximum tolerated dose, or maximum dose according to the local label) Fixed (25mg) ITT: No Followup (wks): 80  NR/unclear |  | Def:CVD mortality Other CVD mortality (fata MI) Incidence p  Incidence p |  |  |
| Rigby, 2009[137](#_ENREF_137)  RCT | Grp1: Metformin + rosiglitazone  Fixed  NS; Mean: 4 mg  Grp2: Metformin + sitagliptin  NS: Mean: 100 mg |  |  | Def: Transient ischemic cerebrovascular accident  Grp1: 1 (2)  Grp2: 0 (0) |  |
| Roden, 2013[139](#_ENREF_139)  RCT | Grp1: Sitagliptin Fixed (100 mg) Grp2: Empagliflozin Fixed (10 mg) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  | Def:CVD mortality Other CVD mortality (cardiovascular death (ICD-10 I00 â€“I99)) Incidence Grp1: 169   p RH 1 Incidence Grp2: 207   p RH 1.5 |  |  |
| Roden, 2013[139](#_ENREF_139)  RCT | Grp1: Sitagliptin Fixed (100 mg) Grp2: Empagliflozin Fixed (25 mg) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  | Def:CVD mortality Other CVD mortality (cardiovascular death (ICD-10 I00 â€“I99)) Incidence Grp1: 827   p RH 1 Incidence Grp2: 876   p RH 1.14 |  |  |
| Roden, 2013[139](#_ENREF_139)  RCT | Grp1: Sitagliptin Fixed (100 mg) Grp2: Empagliflozin Fixed (10 mg) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  | Def:CVD mortality Other CVD mortality (cardiovascular death (ICD-10 I00 â€“I99)) Incidence Grp1: 827   p RH 1 Incidence Grp2: 559   p RH 1.25 |  |  |
| Roden, 2013[139](#_ENREF_139)  RCT | Grp1: Sitagliptin Fixed (100 mg) Grp2: Empagliflozin Fixed (25 mg) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  | Def:CVD mortality Other CVD mortality (cardiovascular death (ICD-10 I00 â€“I99)) Incidence Grp1: 169   p RH 1 Incidence Grp2: 115   p RH 1.63 |  |  |
| Rosenstock, 2006[140](#_ENREF_140)  RCT | Grp1: Metformin  Varied, glucose: 6.1 mmol/l  Start: 500 mg, Mean: 1847 mg, Max: 2000 mg  D: 32 wks  Grp2: Rosiglitazone  Varied, glucose: 6.1 mmol/l  Start: 4 mg, Mean: 7.7 mg, Max: 8 mg  D: 32 wks | Grp1: 0 (0)  Grp2: 0 (0) |  | Def: Not defined ischemic heart disease  Grp1: 2 (1)  Grp2: 2 (1) |  |
| Rosenstock, 2006[140](#_ENREF_140)  RCT | Grp1: Metformin  Varied, glucose: 6.1 mmol/l  Start: 500 mg, Max: 2000 mg, Mean: 1847 mg  D: 32 wks  Grp2: Metformin + rosiglitazone  Varied, glucose: 6.1 mmol/l  Start: 500 mg, Mean: 1799 mg, Max: 2000 mg; Start: 2 mg, Max: 8 mg, Mean: 7.2mg  D: 32 wks | Grp1: 0 (0)  Grp2: 0 (0) |  | Def: Not defined ischemic heart disease  Grp1: 2 (1)  Grp2: 1 (1) |  |
| Rosenstock, 2013[144](#_ENREF_144)  RCT | Grp1: Metformin + placebo Not specified (prestudy dose: ΓëÑ1500 mg/day or maximum tolerated dose) Grp2: Metformin + sitagliptin Not specified (prestud dose: ΓëÑ1500 mg/day or maximum tolerated dose) Fixed (100mg) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  | Def:CVD mortality Other CVD mortality (cardiovascular death (ICD-10 I00 â€“I99)) Incidence Grp1: 827   p RH 1 Incidence Grp2: 2251   p RH 1.28 |  |  |
| Rosenstock, 2013[144](#_ENREF_144)  RCT | Grp1: Metformin + placebo Not specified (prestudy dose: ΓëÑ1500 mg/day or maximum tolerated dose) Grp2: Metformin + empagliflozin Not specified (prestudy dose: ΓëÑ1500 mg/day or maximum tolerated dose) Fixed (10mg) ITT: Not applicable (e.g., cohort) Followup (wks):   NR/unclear |  | Def:CVD mortality Other CVD mortality (cardiovascular death (ICD-10 I00 â€“I99)) Incidence Grp1: 169   p RH 1 Incidence Grp2: 591   p RH 1.32 |  |  |
| Rosenstock, 2013[144](#_ENREF_144)  RCT | Grp1: Metformin + placebo Not specified (prestudy dose: ΓëÑ1500 mg/day or maximum tolerated dose) Grp2: Metformin + empagliflozin Not specified (prestudy dose: ΓëÑ1500 mg/day or maximum tolerated dose) Fixed (25mg) ITT: Yes Followup (wks): 44 |  | Def:CVD mortality Composite CVD mortality outcome (fatal acute myocardial infarction and cario-respiratory arrest) Incidence Grp1: 1    Incidence Grp2: 1 |  |  |
| Rosenstock, 2013[144](#_ENREF_144)  RCT | Grp1: Metformin + sitagliptin Not specified (prestud dose: ΓëÑ1500 mg/day or maximum tolerated dose) Fixed (100mg) Grp2: Metformin + empagliflozin Not specified (prestudy dose: ΓëÑ1500 mg/day or maximum tolerated dose) Fixed (10mg) ITT: Yes Followup (wks): 76 |  | Def:CVD mortality Other CVD mortality (sudden death, cardiac arrest, coronary artery arteriosclerosis, cardiac failure, AMI) Incidence Grp1: 3    Incidence Grp2: 1 |  |  |
| Rosenstock, 2013[144](#_ENREF_144)  RCT | Grp1: Metformin + sitagliptin Not specified (prestud dose: ΓëÑ1500 mg/day or maximum tolerated dose) Fixed (100mg) Grp2: Metformin + empagliflozin Not specified (prestudy dose: ΓëÑ1500 mg/day or maximum tolerated dose) Fixed (25mg) ITT: Yes Followup (wks): 76 |  | Def:CVD mortality Other CVD mortality (sudden death, cardiac arrest, coronary artery arteriosclerosis, cardiac failure, AMI) Incidence Grp1: 3    Incidence Grp2: 0 |  |  |
| Ross, 2012[146](#_ENREF_146)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1963.6mgMax: 1500mg or maximum tolerated dose) Grp2: Metformin + linagliptin + placebo Fixed (Mean: 1811.6mgMax: 1500mg or maximum tolerated dose) Fixed (5mg) ITT: Yes Followup (wks): 76 |  | Def:CVD mortality Other CVD mortality (sudden death, cardiac arrest, coronary artery arteriosclerosis, cardiac failure, AMI) Incidence Grp1: 3    Incidence Grp2: 2 |  |  |
| Ross, 2012[146](#_ENREF_146)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1963.6mgMax: 1500mg or maximum tolerated dose) Grp2: Metformin + linagliptin + placebo Fixed (Mean: 1811.6mgMax: 1500mg or maximum tolerated dose) Fixed (5mg) ITT: Yes Followup (wks): 76 |  | Def:CVD mortality Other CVD mortality (sudden death, cardiac arrest, coronary artery arteriosclerosis, cardiac failure, AMI) Incidence Grp1: 1    Incidence Grp2: 0 |  |  |
| Ross, 2012[146](#_ENREF_146)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1963.6mgMax: 1500mg or maximum tolerated dose) Grp2: Metformin + linagliptin + placebo Fixed (Mean: 1811.6mgMax: 1500mg or maximum tolerated dose) Fixed (5mg) ITT: Yes Followup (wks): 76 |  | Def:CVD mortality Other CVD mortality (sudden death, cardiac arrest, coronary artery arteriosclerosis, cardiac failure, AMI) Incidence Grp1: 1    Incidence Grp2: 2 |  |  |
| Ross, 2012[146](#_ENREF_146)  RCT | Grp1: Metformin + placebo Fixed (Mean: 1963.6mgMax: 1500mg or maximum tolerated dose) Grp2: Metformin + linagliptin + placebo Fixed (Mean: 1811.6mgMax: 1500mg or maximum tolerated dose) Fixed (5mg) ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Composite CVD mortality outcome (cardiac failure, myocardial infarction) Incidence Grp1: 1    Incidence Grp2: 1 |  |  |
| Roumie, 2012[210](#_ENREF_210)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Not applicable (e.g., cohort) Followup (wks): |  | Def:CVD mortality Other CVD mortality (death from cardiovascular causes (ICD- 10 codes I00â€“I99)) Incidence Grp1: 109  1533 Person-years p 0.79 Incidence Grp2: 1378  9570 Person-years p 1 REF |  |  |
| Roumie, 2012[210](#_ENREF_210)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified      ITT: Not applicable (e.g., cohort) Followup (wks): |  | Def:CVD mortality Other CVD mortality (death from cardiovascular causes (ICD- 10 codes I00â€“I99)) Incidence Grp1: 109  1533 Person-years p 0.79 Incidence Grp2: 447  4280 Person-years p 0.94 |  |  |
| Roumie, 2012[210](#_ENREF_210)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Not applicable (e.g., cohort) Followup (wks): |  | Def:CVD mortality Other CVD mortality (death from cardiovascular causes (ICD- 10 codes I00â€“I99)) Incidence Grp1: 1378  9570 Person-years p 1 REF Incidence Grp2: 447  4280 Person-years p 0.94 |  |  |
| Roumie, 2012[210](#_ENREF_210)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Other CVD mortality (sudden cardiac death or worsening CAD) Incidence Grp1:    Incidence Grp2: |  |  |
| Roumie, 2012[210](#_ENREF_210)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Other CVD mortality (sudden cardiac death or worsening CAD) Incidence Grp1:    Incidence Grp2: |  |  |
| Roumie, 2012[210](#_ENREF_210)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: SU Not specified   ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Other CVD mortality (sudden cardiac death or worsening CAD) Incidence Grp1: 1    Incidence Grp2: |  |  |
| Russell-Jones, 2012[147](#_ENREF_147)  RCT | Grp1: Metformin + placebo Titrated (Max: 2500 mg based on glycemic controltarget 2000 mg) Grp2: Pioglitazone + placebo Titrated (Max: 45 mgtarget dose 45 mg/d) ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Other CVD mortality (sudden cardiac death or worsening CAD) Incidence Grp1:    Incidence Grp2: 1 |  |  |
| Russell-Jones, 2012[147](#_ENREF_147)  RCT | Grp1: Metformin + placebo Titrated (Max: 2500 mg based on glycemic controltarget 2000 mg) Grp2: Sitagliptin + placebo Fixed (100 mgimplies fixed daily dose and makes sense clinically for sita) ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Other CVD mortality (sudden cardiac death or worsening CAD) Incidence Grp1: 1    Incidence Grp2: 1 |  |  |
| Russell-Jones, 2012[147](#_ENREF_147)  RCT | Grp1: Metformin + placebo Titrated (Max: 2500 mg based on glycemic controltarget 2000 mg) Grp2: Exenatide + placebo Fixed (2.0 mg subcut weeklyEQW) ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Other CVD mortality (sudden cardiac death or worsening CAD) Incidence Grp1:    Incidence Grp2: 1 |  |  |
| Russell-Jones, 2012[147](#_ENREF_147)  RCT | Grp1: Pioglitazone + placebo Titrated (Max: 45 mgtarget dose 45 mg/d) Grp2: Sitagliptin + placebo Fixed (100 mgimplies fixed daily dose and makes sense clinically for sita) ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Other CVD mortality (sudden cardiac death or worsening CAD) Incidence Grp1:    Incidence Grp2: |  |  |
| Russell-Jones, 2012[147](#_ENREF_147)  RCT | Grp1: Pioglitazone + placebo Titrated (Max: 45 mgtarget dose 45 mg/d) Grp2: Exenatide + placebo Fixed (2.0 mg subcut weeklyEQW) ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Other CVD mortality (sudden cardiac death or worsening CAD) Incidence Grp1:    Incidence Grp2: |  |  |
| Russell-Jones, 2012[147](#_ENREF_147)  RCT | Grp1: Sitagliptin + placebo Fixed (100 mgimplies fixed daily dose and makes sense clinically for sita)   Grp2: Exenatide + placebo Fixed (2.0 mg subcut weeklyEQW)   ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Other CVD mortality (sudden cardiac death or worsening CAD) Incidence Grp1: 1    Incidence Grp2: |  |  |
| Scheller, 2014[211](#_ENREF_211)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Sitagliptin Not specified   ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Other CVD mortality (sudden cardiac death or worsening CAD) Incidence Grp1:    Incidence Grp2: 1 |  |  |
| Scheller, 2014[211](#_ENREF_211)  Retrospective cohort | Grp1: Metformin Not specified   Grp2: Sitagliptin Not specified   ITT: Yes Followup (wks): 104 |  | Def:CVD mortality Other CVD mortality (sudden cardiac death or worsening CAD) Incidence Grp1:    Incidence Grp2: |  |  |
| Schernthaner, 2015[148](#_ENREF_148) | Grp1: Metformin + glimepiride + placebo  Mean: 1572 mg/d  Titrated (Mean: 3.3 mg/d Max: 6mg/d)  Grp2: Metformin + saxagliptin + placebo  Mean: 1647  Fixed (5 mg/d)  ITT: No  Followup (wks): 52 | Def: All-cause mortality  Incidence Grp1: 1  Incidence Grp2: 1 | Fatal MI  Incidence Grp1: NR  Incidence Grp2: 1 |  |  |
| Schernthaner, 2004[149](#_ENREF_149)  RCT | Grp1: Metformin  Varied  Max: 850 mg tid  Grp2: Pioglitazone  Varied  Start: 30 mg, Max: 45 mg | Grp1: 2 (0.3)  Grp2: 3 (0.5) |  |  |  |
| Schumm-Draeger, 2015[151](#_ENREF_151) | Grp1: Metformin + placebo  Fixed (adjusted to 1500, 2000, 2500 mg/d)  Grp2: Metformin + dapagliflozin  Fixed 5 mg twice daily | Grp1: 0 (0)  Grp2: 0 (0) |  |  |  |
| Schumm-Draeger, 2015[151](#_ENREF_151) | Grp1: Metformin + placebo  Fixed (adjusted to 1500, 2000, 2500 mg/d)  Grp2: Metformin + dapagliflozin  Fixed 10 mg/d | Grp1: 0 (0)  Grp2: 0 (0) |  |  |  |
| Seck, 2010[154](#_ENREF_154)  RCT | Grp1: Metformin + sitagliptin  Fixed  Grp2: Metformin + glipizide  Fixed; Varied, glucose > 110 mg/dl  NR; Start: 5 mg, Max: 20 mg, Mean: 9.2 mg | Grp1: 8 (1.4)  Grp2: 1 (0.2) | Def: Sudden cardiac death  Grp1: 2 (<1)  Grp2: 0 (0) |  |  |
| St John Sutton, 2002[159](#_ENREF_159)  RCT | Grp1: Rosiglitazone  Fixed  Start: 4 mg bid  Grp2: Glyburide  Varied  Max: 20 mg |  |  | Def: CVD morbidity/heart disease  Grp1: 9 (9)  Grp2: 5 (5) |  |
| Stewart, 2006[160](#_ENREF_160)  RCT | Grp1: Metformin  Varied  Start: 500 mg, Mean: 2627.9 mg, Max: 3000 mg  D: 20wks  Grp2: Metformin + rosiglitazone  Varied  Start: 500 mg, Mean: 1812.9 mg, Max: 2000 mg  D: 18 wks |  |  | Def: MI, angina pectoris, myocardial ischemic, coronary artery insufficiency  Grp1: 0 (0)  Grp2: 4 (2) |  |
| van der Meer, 2009[172](#_ENREF_172)  RCT | Grp1: Metformin + glimepiride  Fixed  Start: 1000 mg, Max: 2000 mg; Start: 15 mg, Max: 30 mg  D: 8 wks  Grp2: Pioglitazone + glimepiride  Varied  Not specified  D: 8 wks |  | Def: CVD event  Grp1: 0 (0)  Grp2: 0 (0) |  |  |
| Wang, 2015[173](#_ENREF_173)  RCT | Grp1: Metformin + placebo  Fixed >=1500 mg/day or maximum tolerated dose  Grp2: Metformin + lingliptin  Fixed >=1500 mg/day or max tolerated dose  Fixed 5mg |  |  | Nonfatal MI (suspected Myocardial Ischemia)  Incidence Grp1: 0  Incidence Grp2: 1 | Nonfatal stroke (lacunar infarction)  Incidence Grp1: 1  Incidence Grp2: 0 |
| Weissman, 2005[174](#_ENREF_174)  RCT | Grp1: Metformin  Varied  Start: 1000mg, Max: 2000mg  Grp2: Metformin + rosiglitazone  Fixed; Varied  Start: 1000 mg; Start: 4 mg, Max: 8 mg | Grp1: 0 (0)  Grp2: 1 (<1) |  | Def: CVD morbidity/MI (non-fatal)  Grp1: 0 (0)  Grp2: 2 (1) |  |
| Weissman, 2005[174](#_ENREF_174)  RCT | Grp1: Metformin  Varied  Start: 1000mg, Max: 2000mg  Grp2: Metformin + rosiglitazone  Fixed; Varied  Start: 1000 mg; Start: 4 mg, Max: 8 mg |  |  | Def: CVD morbidity/MI (non-fatal) + pulmonary edema with MI  Grp1: 3 + 1 withdrew (1)  Grp2: 5 (1) |  |
| Xu, 2015[178](#_ENREF_178) | Grp1: Pioglitazone  Titrated 45 mg/d  Grp2: Exenatide  Titrated 10ug twice daily |  |  |  | Def: Other cerebrovascular (cerebral infarction)  Grp1:NR(1)  Grp2: NR(1) |

ACEI = angiotensin-converting enzyme inhibitors; ADA = American Diabetes Association; ALT = alanine aminotransferase; AST = asparate aminotransferase; BG = blood glucose, BMI = body mass index; BP = blood pressure; CAD = coronary artery disease; CHF = congestive heart failure; CK = creatine phosphokinase; CVD = cardiovascular diseases; DBP = diastolic blood pressure; DM = diabetes mellitus; FBG = fasting blood glucose; FPG = fasting plasma glucose; g/day = grams per day; g/dl = grams per deciliter; GFR = glomerular filtration rate; GI r = gastrointestinal; HbA1c = hemoglobin A1c; kg = kilogram; kg/m2 = kilograms per meter squaredlbs = pounds; LDL = low density lipoprotein; LVEF = left ventricular ejection fraction; met = metformin; mg = milligram; mg/d = milligrams per day; mg/dL = milligrams per deciliter; MI = myocardial infarction ; mm Hg = millimeters of mercury; mmol/l =millimoles per liter; NCEP ATP III = National Cholesterol Education Program Adult Treatment Panel IIIng/ml = nanograms per milliliter; nmol/l = nanomoles per liter; NR = Not Reported; NYHA = New York Heart Association; ODM = oral diabetes medications; pmol/l = picomoles per liter; SBP = systolic blood pressure; SGOT = serum glutamyl oxaloacetic transaminase; SGPT = serum glutamyl pyruvic transaminase; SU = sulfonylurea; TIA = Transient ischemic attack; TZD = thiazolidinedione; U/kg = units per kilogram; UKPDS = The UK Prospective Diabetes Study; US = United States; WHO = World Health Organization; yrs = years

Some data may have not been extracted because the question was not asked.